24
General
657

Notified in Army Orders for November, 1942

THE WAR OFFICE

MEMORANDA ON MEDICAL DISEASES IN TROPICAL AND SUB-TROPICAL AREAS

1942

LONDON
HIS MAJESTY'S STATIONERY OFFICE

Price 3s. 6d. net

... *in Army Orders for* 30*th November*, 1942

General
657

THE WAR OFFICE

MEMORANDA ON MEDICAL DISEASES IN TROPICAL AND SUB-TROPICAL AREAS

1942

(Reprinted May, 1943, incorporating Amendment No. 1)

1943
Price 3s. 6d. net

By Command of the Army Council,

[signature]

THE WAR OFFICE,
30*th November*, 1942.

LIST OF CONTENTS

PREFACE

These Memoranda were originally compiled by the late Sir Andrew Balfour, K.C.M.G., C.B., F.R.S., for medical officers serving abroad in the war of 1914–18. He and his collaborators prepared two further editions and the work continued to expand under the editorship of Lieutenant-General Sir William MacArthur, K.C.B., D.S.O., O.B.E. This, the seventh, edition contains new articles on Cerebrospinal fever, Lymphopathia venereum, Pellagra, Rabies, Rat-bite fever, and Sickle-celled anæmia, while the Rickettsial Infections have been brought together under a single heading. It is therefore larger and more comprehensive ; but, like its predecessors, it does not claim to be more than a series of miscellaneous memoranda arranged in alphabetical order ; and, like the first edition, it is primarily designed to give practical help to a large number of medical officers who find themselves unexpectedly confronted, in time of war, by the problems of hot countries.

Many of the illustrations have been lent by the Wellcome Bureau of Scientific Research, and the book has always owed much to the help of Dr. C. M. Wenyon, C.M.G., C.B.E., F.R.S., Director of the Bureau.

ALEX. HOOD,
Lieutenant-General,
Director-General,
Army Medical Services.

October, 1942.

ANCYLOSTOMIASIS

This important helminthic infection prevails wherever climatic conditions and imperfect sanitation permit the development of ancylostomes. The disease is widely distributed between the latitudes of 30 deg. N. and 30 deg. S., and beyond these limits it has been found among workers in mines and tunnels, owing to the higher temperature in such places, and the lack of sanitary control.

Etiology.—Human ancylostomiasis is due mainly to two species of nematode worms belonging to different genera of the family Ancylostomidæ. One of these species is *Ancylostoma duodenale*, the other *Necator americanus*. Their respective distribution is difficult to demarcate as they have often been confused in the past. In most affected countries both species occur, and they may be present in the same person. Other factors being equal, *A. duodenale* appears to be more hurtful to its host than *N. americanus*. Cases of human infection with *A. braziliense* (=*ceylanicum*) have been recorded, and a mild degree of such infestation is stated to be not uncommon in India.

The ancylostomes are small worms, about 8–10 mm. long, of a pinkish-white colour when alive, but grey when dead. When gorged with blood they are reddish brown. Male and female forms are present and their habitat is the human small intestine, more especially the jejunum, though they are also found in the duodenum and rarely in the ileum. Ancylostomes attach themselves to the mucous membrane by means of their buccal armature, more formidable in the case of *A. duodenale*. Its mouth capsule possesses both dorsal and ventral hooked teeth, while in *N. americanus* the solitary so-called " tooth " is dorsal. The latter has the teeth proper replaced by chitinous plates. Each species is also armed with internal buccal lancets.

In *A. braziliense*, the outer pair of ventral teeth are large and well developed, whereas the inner pair are minute.

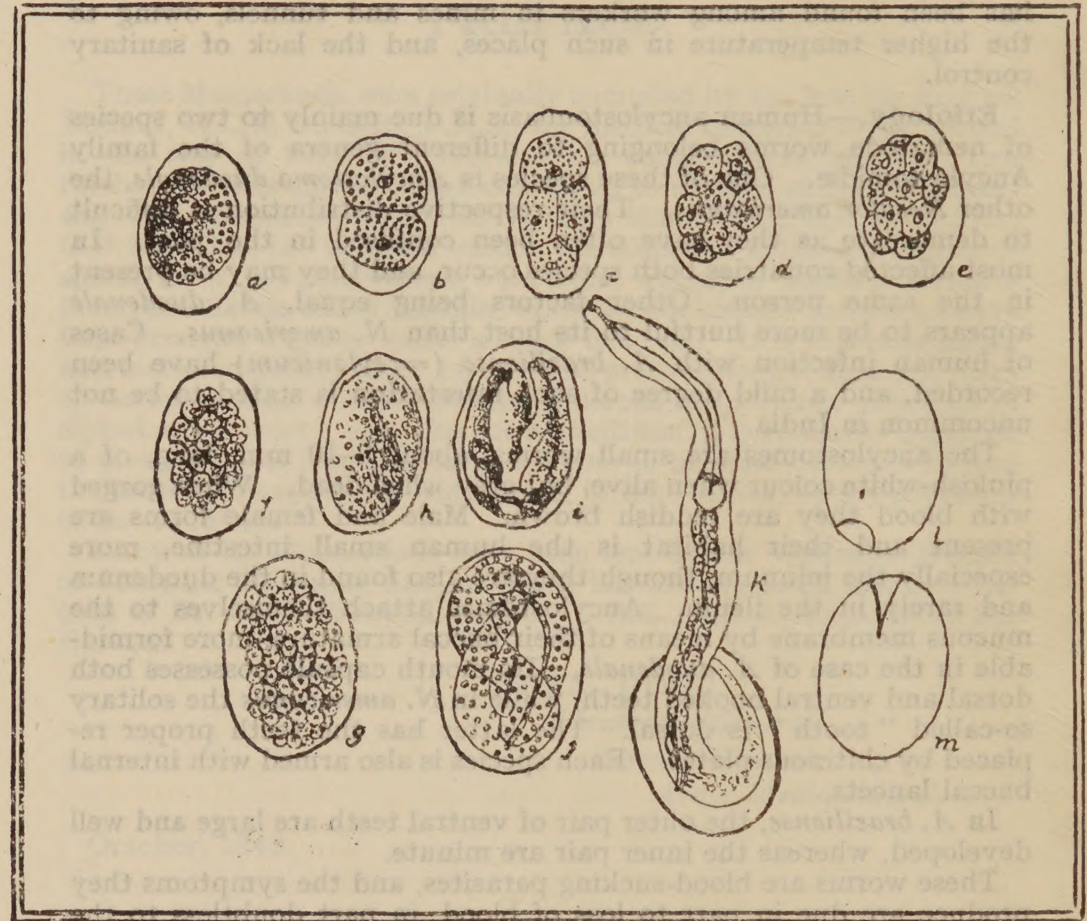
These worms are blood-sucking parasites, and the symptoms they produce are due in part to loss of blood, in part doubtless to the slow destruction of the mucosa and submucosa on which the ancylostomes feed, and possibly also to the effects of a hæmolytic toxin which they are believed to excrete. It has also been said that bacterial infections may result through the lesions caused by the parasites and that these play an important part in the symptomatology.

A certain amount of development occurs as the egg travels down the human alimentary canal, for the contained granular mass divides into two and then into four segments. It is at this latter stage that the egg is usually found in the fæces (Plate 1).

Air, moisture and heat are required for further development, which is most rapid when the temperature is at 25 deg. to 35 deg. C.

(77 deg. to 95 deg. F.). In twenty-four hours, if the conditions are favourable, the young embryo can be seen coiled up in the egg. It escapes from it as a larva in from two to seven days and feeds upon the fæces (Fig. 1). The larva moults twice, and often after the second moult it retains the cast skin as a sheath, but this may be discarded. It has now reached the infective stage and, ceasing to feed and grow, it makes for moist earth or water. It is active and can swim, wriggle, and even climb up any surface which is wet,

Fig. 1.



Development of *Ancylostoma duodenale*: *a, b, c, d, e, f, g*, segmentation of egg; *h, i, j*, the larva; *k*, escape of larva from egg; *l, m*, empty egg-shell. Greatly enlarged. (After Perroncito.)

and it is greatly assisted in its progression by the presence of an accompanying film of water. Larvæ may pass vertically through as much as thirty-six inches of light soil to reach the surface of the ground, but their radial spread from a focus of infection seems to be limited to a few inches.

Infection can take place in two ways, through the mouth and through the skin. The latter is much the more important, though direct transference through the mouth may occur as in the case of

infected drinking water, food, especially vegetables, or food vessels contaminated by mud containing the larvæ and amongst earth-eaters or children who carry dirt to their mouths. The skin route is by way of the hair follicles through which the larvæ pass, and from the subcutaneous tissues they reach the veins and lymphatics and travel to the intestine via the heart, arteries, capillaries, and air cells of the lung, bronchi, trachea, larynx, œsophagus and stomach. Leaving the stomach, they mature in the intestine, and, after copulation, the female produces eggs which appear in the fæces seven to ten weeks after infection. There is evidence to show that an alternative route from the lungs is also, though more rarely, followed, namely, by the pulmonary artery to the pulmonary veins and in the general blood stream to the jejunum, where the mucosa is pierced and the larvæ reach the lumen of the bowel.

The adult worms may remain alive in the intestine, in diminishing numbers, for as long as six years.

Symptoms.—As the ancylostomes present vary greatly in numbers the symptoms naturally also vary in different cases. Other factors in variability are personal idiosyncrasy to the action of the toxin and the presence of associated diseases. In the main the symptomatology is that of a secondary anæmia.

There are cryptic, mild, and severe types. In the first variety the disease can only be definitely diagnosed by the finding of ova in the stools. Such cases are rather ancylostome carriers than victims of ancylostomiasis, but careful inquiry will often show some slight digestive trouble with tenderness and pain and discomfort in the epigastrium. There may be a slight reduction in the hæmoglobin content of the blood and a trifling loss in the power of mental concentration. It may be said of such cases that they do not know they have been ill until they are cured. They notice the difference in their health when freed from their worms. A blood examination may reveal eosinophilia and suggest an examination of the fæces. It has been stated that 500 worms must be present for six months before effects are produced on the host.

The mild cases present moderate anæmia, and epigastric tenderness is a marked feature often associated with acid dyspepsia. The ingestion of food frequently, if temporarily, relieves the painful sensations. The patient may suffer from cardiac palpitation and shortness of breath.

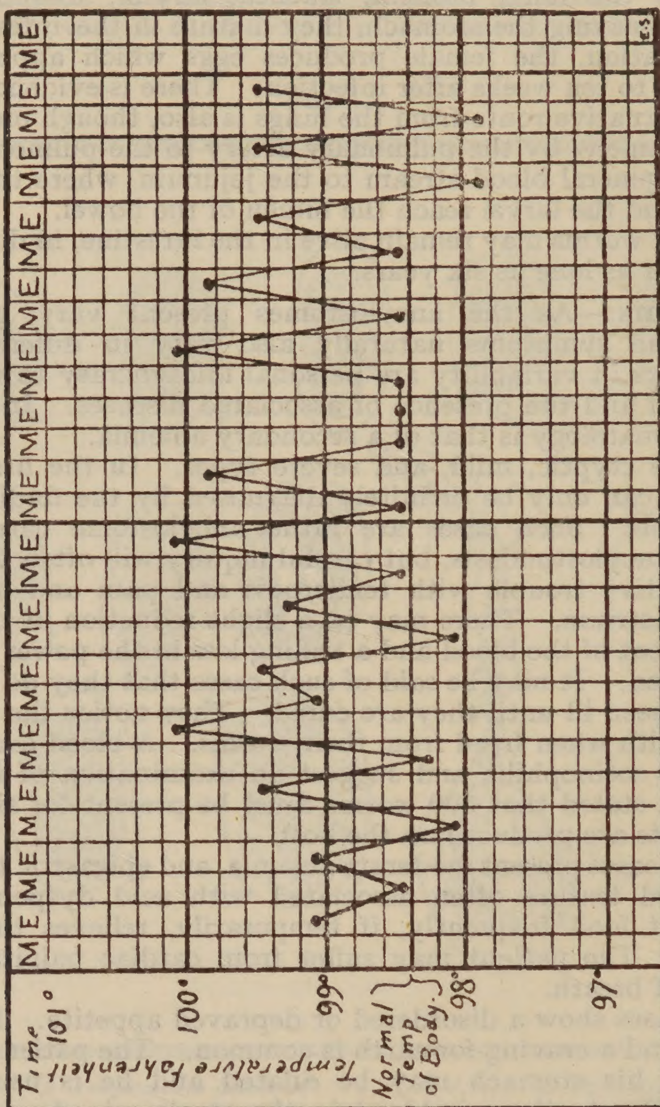
Severe cases show a disordered or depraved appetite. It is often ravenous, and a craving for earth is common. The patient becomes pot-bellied, his stomach may be dilated and he is usually constipated. Rarely there is blood in the stools mixed up with the fæces.

Physical and mental fatigue ensue, together with various nervous symptoms and joint pains. As the anæmia progresses the palpitation and dyspnœa increase. Œdema shows itself in advanced cases chiefly about the face and ankles ; a puffy face is not uncommon and ascites may occur. The patient rather resembles a man suffering from chronic nephritis. In white patients the skin, which is dry, assumes an earthy hue, and attention has been drawn to the peculiar dead-white appearance of the conjunctiva of the lower lid.

It is important to note that ancylostomiasis may apparently be a

cause of jaundice and of liver enlargement and that it is often accompanied by fever, which varies in character (Fig. 2). The latter is usually irregular and intermittent and is said to be of bacterial origin, intestinal organisms gaining access to the blood through the wounded mucosa. There is no change in the spleen. Emaciation is not a feature of the disease in adults.

Fig. 2.



Ancylostomiasis Fever.
(Chalmers and Castellani.)

So much for the general symptoms. In the tropics anæmia plus dropsy should always lead one to think of ancylostomiasis. As regards the skin eruption at the site of invasion, it suffices to say that at the start it is a mild dermatitis characterized by redness and the presence of urticarial weals or small vesicles, and that later, owing to secondary pyogenic infection, it assumes a pustular character. It is known as ground-itch.

Complications.—Ulceration of the mouth may be noted. The disease often occurs along with malaria and amœbic dysentery.

Diagnosis.—This can only be made with certainty by the discovery of ova in the fæces, though it must be remembered that their absence does not exclude ancylostomiasis, for symptoms may persist though the parasites have disappeared spontaneously or have been expelled. If ova are not found on direct examination and if the more elaborate concentration methods, such as that of Clayton Lane, are not feasible, it is not a bad plan to place washed and sedimented fæces on a slide for a few minutes and then gently immerse in water. The ova remain after everything else has been washed off, and by repeating the process quite a collection of eggs may be obtained on the slide.

The eggs of such nematodes as *Trichostrongylus colubriformis* and *Ternidens deminutus*, which occasionally parasitize man, may readily be mistaken for those of ancylostomes. In doubtful cases a series of eggs should be measured, and the degree of development in the yolk of freshly passed specimens carefully noted.

The presence of eosinophilia is usually a valuable indication of ancylostomiasis, but severe cases, or those complicated by malaria or kala-azar, may show no increase in the eosinophiles.

Differential Diagnosis.—Distinguish from Bright's disease, beriberi and rheumatism. Do not confound ancylostome fever with malaria and other tropical pyrexias, or ancylostomiasis with splenomegaly for kala-azar. Severe ascaris infection may simulate ancylostomiasis.

Prophylaxis.—From what has been said it must be evident that the chief prophylactic measure consists in preventing the fæcal contamination of soil, water, or of such foodstuffs as vegetables which are eaten uncooked.

Special care as regards conservancy methods in the tropics is therefore of prime importance.

The employment of the deep bore-hole latrine affords an adequate method of disposal of fæces, and is preferable to trenching systems. In either case care must be taken to see that the edges of surfaces around the latrine openings are kept clean and that the feet of users are protected.

Bucket removal systems are less satisfactory but may have to be employed under certain circumstances. Cresol should be placed in the latrine buckets in the usual way or, if this is not available, a layer of common salt on the bottom of the bucket and another on the top when the bucket is full, will serve the same purpose. In the latter case intimate contact with the fæces must be ensured by mixing, as solid salt does not penetrate fæces for some 48 hours.

If incineration is employed there must be no mixing of the fresh fæces with bhoosa or other combustible matter on the ground, thereby increasing the risk of soil contamination. From the pan to the fire must be the motto.

Contaminated soil is the most important source of infection, and such contamination may be direct or indirect, the latter often occurring owing to dissemination by footwear. Over three hundred larvæ have been recovered from the muddy shoes of one person. Ova, too, may pass unaffected through the stomach and intestine of the domestic pig and may be disseminated in this way.

Camping sites must be carefully selected and kept clean. Contamination of ground may be established by the finding of larvæ and an apparatus for their detection has been devised. It consists of a funnel covered by a fine mesh sieve in which the soil is placed. When the funnel is filled with water up to the lower soil level the larvæ pass into the water and can be recovered from the lower end of the funnel.

Badly contaminated ground should be abandoned, but as most of the larvæ are found near the surface of the ground and are usually localized in their lateral distribution, less seriously affected areas may be treated by digging up to a depth of eighteen inches and applying 2 per cent. boiling cresol solution or an 8 per cent. solution of common salt. If these measures are impossible the suspected ground may be "fired" before use.

Owing to the need of the larvæ for moisture the drying up of damp areas by drainage often achieves good results.

Water supplies should be protected and bathing places properly chosen and regulated, while all measures necessary must be taken to prevent contamination of foodstuffs such as vegetables and fruits which are eaten uncooked.

The protection of the individual must be given careful consideration. Boots and sandals, if not defective, protect to a great extent, but it must be remembered that when not on the march native troops may discard their boots and in this way may convey infection.

Many Indian and African troops already suffer from mild degrees of the disease or at least harbour parasites.

In civil communities an important prophylactic measure is the freeing of carrier cases and of those who suffer from ancylostomiasis from their parasites, in other words, the extermination of the mature worm; but this cannot be done on a large scale in the case of a field force.

Treatment.—The cheapest and safest anthelmintic in the treatment of ancylostomiasis is tetrachlorethylene, which may be given in a single dose of 4 c.cm. The addition of 1 c.cm. of oil of chenopodium renders the mixture more effective. The drug is best administered in the early morning on an empty stomach. No food should be given until there is a satisfactory bowel movement. A dose of Epsom salts may be given if the bowels do not act within four hours.

Tetrachlorethylene is also effective against *Enterobius*, but not against *Trichuris*.

Carbon tetrachloride is also an effective anthelmintic, but its use is not free from danger.

Fatalities have followed the administration of impure preparations, but the drug, even when certified by reliable chemists to be free from contamination, has caused death, presumably by acting on a liver already diseased. Therefore carbon tetrachloride should never be used for treating known alcoholics. It has been pointed out that the dose usually recommended is double the minimum lethal dose, a unique example in therapeutics, and this probably explains the accidents which happen more frequently than are recorded. In poisonous doses, carbon tetrachloride causes a central lobular necrosis of the liver with fatty degeneration which may begin even

within four hours of administration. The clinical evidences of poisoning are vomiting, liver tenderness and pain, jaundice, hæmaturia and temporary suppression of urine. Treatment consists in the administration of glucose, either intravenously in a 5 per cent. solution, of which several hundred c.cm. may be given, or in drachm doses by the mouth.

0·2 c.cm. of carbon tetrachloride, in gelatine capsules, in water, or emulsified in skimmed milk, may be given for each year of age up to a maximum of 4 c.cm., the ordinary dose for an adult being 3 c.cm. This is usually administered early in the morning, the patient taking no breakfast that day. The drug may act as its own purge, but it is advisable to follow the carbon tetrachloride by a dose of magnesium sulphate about three hours later. This may prevent headache, giddiness and other unpleasant symptoms. Food should be withheld until the purgative has acted freely.

Carbon tetrachloride is very effective for threadworms, and is of some value in *Ascaris* infection ; it is useless against *Trichuris, Strongyloides*, and tapeworm.

Oil of chenopodium has been used with success in many ancylostome campaigns.* The medicinal properties of this drug depend on the contained ascaridol, but the chemical composition of the oil is not constant, so that a dose recommended as the optimum for treatment may not always give equally satisfactory results.

Oil of chenopodium is best given in gelatine capsules filled a few hours before use, or may be taken in emulsion or in water. Some prefer to administer the dose on an empty stomach, the patient taking no food on the morning of the treatment. Others hold that full diet lessens the toxicity of the drug and does not lessen its efficacy. The maximum dose is 3 c.cm., but smaller amounts are usually administered. Excellent results have been obtained by three 0·5 c.cm. doses given at intervals of an hour, and followed by a dose of magnesium sulphate about two hours later. Two such treatments have been claimed to remove 99 per cent. of worms. Another method is to give the oil in one single dose of 2 c.cm., followed by a saline purge as before.

Oil of chenopodium is effective against *Ascaris* and *Strongyloides*.

Narcosis and other ill-effects have followed the administration of the oil and cumulative effects have been noted, so it must be given with care, especially in debilitated persons. The treatment should not be repeated under ten days. There is no chemical antidote. In cases of poisoning digitalis and adrenaline have been found useful. Caffeine does harm.

Oil of chenopodium may be combined with carbon tetrachloride, one part of the former to two of the latter. 0·1 c.cm. of the mixture is given for each year of age up to 1·5 c.cm. The dose is divided into two equal parts taken in water at an interval of one or two hours. Two hours after the second dose a saline purge is given.

Remember that the passage of worms after anthelmintic treatment is an indication for continuing rather than stopping treatment. Cessation of treatment should depend on the disappearance of

---

* Ascaridol, the active principle of oil of chenopodium, is also an effective anthelmintic.

symptoms and the negative results of later microscopical examinations.

The anæmia must be treated by iron and other tonics and a nutritious and easily assimilable diet prescribed.

Ground-itch is best treated by an ointment containing zinc oxide and salicylic acid. Bad cases may require antiseptic dressings.

SOME

ARTHROPOD PESTS *

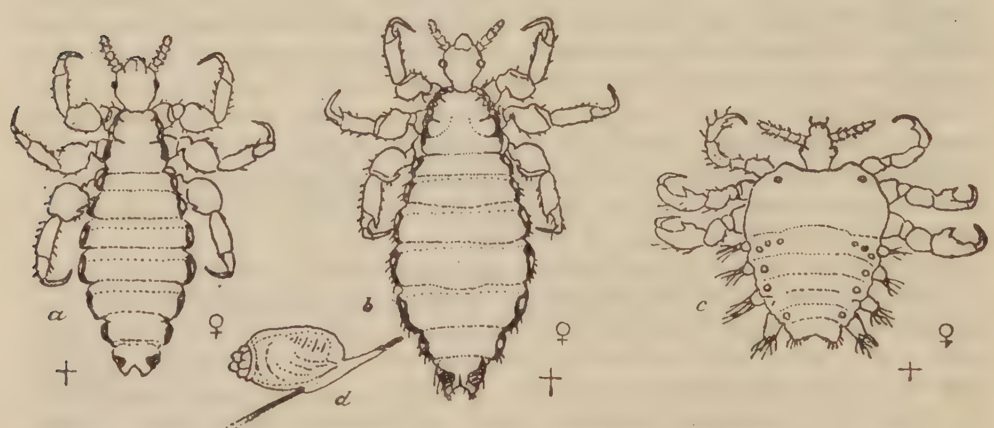
WINGLESS PESTS

Under this heading the following arthropods are included :— Lice, Bugs, Fleas, the Itch Mite, Ticks and Ants.

LICE

The lice, of which man is the natural host, comprise two species, *Pediculus humanus* (head and body lice) and *Phthirus pubis* (crab lice) (Fig. 3). Head lice and body lice are now regarded as varieties of *Pediculus humanus*, and not as two distinct species. Consequently, if it is desired to separate these two sub-species a trinominal designation is necessary, for a binominal label is the badge of a species.

Fig. 3.



a. Pediculus humanus capitis ; *b.* P. humanus corporis ; *c.* Phthirus pubis ; *d.* a louse egg attached to a hair.

Usually *P. humanus capitis* and *P. humanus corporis* can be distinguished by slight morphological differences. The more slender antennal segments of the body louse may be mentioned as probably the most obvious of these. The third antennal segment of a body louse can be seen at a glance to be definitely longer than it is broad, whereas in a head louse the broadest part of this segment is not

* Most of the drawings illustrating this section are reproduced by permission of the Wellcome Bureau of Scientific Research.

strikingly less than the length. On the other hand, specimens of *P. humanus* are found which cannot be assigned definitely to either subspecies.

Diseases transmitted by lice.—Typhus, relapsing fever and trench fever. Lice cause considerable cutaneous irritation, and as a result of scratching, secondary infection may occur, and diseases such as impetigo, infective dermatitis and furunculosis may develop in infested persons. Until these complications develop, general symptoms of toxæmia due to the actual infestation are not usually noted, but if a patient is very heavily infested, general symptoms of a toxic nature may be seen : there is usually a slight but persistent rise of temperature, headache, lethargy and pains in the joints, and a rash resembling German Measles may appear. These symptoms disappear when the patient is loused.*

PEDICULUS HUMANUS CORPORIS

Under ideal conditions the female body louse may lay 10 eggs per diem, and a total number of about 300 in the course of her life. Egg-laying is most active at a temperature of 31° C. (88° F.) and ceases at 20° C. (68° F.). If kept at body temperature (37° C.) the eggs hatch in about six days ; at temperatures above 37° C. (98·6° F.) eggs do not develop, and are killed if a temperature of 40° C. (104° F.) is maintained. Under cold conditions eggs are killed in two hours at a temperature of −17° C. (1·4° F.), and in seven days at a temperature of 5° C. (41° F.). If maintained at a temperature of 22° C. (72° F.) ova do not hatch. The development of the ova may be retarded by variations of temperature and if infested clothing is not worn frequently the hatching may be delayed for as long as 25 days.

The larva which emerges from the egg has a general resemblance to the adult : three moults occur before the adult males and females are formed.

Buxton gives the following data, in which the time-periods are adjusted to allow for fluctuations in temperature, with consequent retardation of development :—

> The egg stage lasts nine days and 30 per cent. of the eggs fail to hatch. The larval stage lasts for nine days and the mortality may be 40 per cent. The female lives for 34 days ; she does not lay eggs on the 1st, 2nd or 34th day, but she may lay nine eggs a day from the third to the thirty-third day inclusive, *i.e.* a total of 279 eggs. Therefore, allowing for the mortality of eggs and larvæ, 100 eggs produce 42 adults.

The geographical distribution of lice is very wide, and there is no part of the world in which the insect (either *corporis* or *capitis*) cannot be found, except for a few localized areas where the inhabitants have maintained a high standard of personal hygiene. The species of lice found on man do not occur on other animals except menagerie monkeys. At ordinary room temperatures (*e.g.* 16° C., 61° F.) in temperate climates they can exist without feeding for a week, but in warmer climates their longevity is shortened and at

* Classical English for the unscholarly neologism "deloused."

temperatures of 30° C. (86° F.) they usually die in two days if removed from their host. Infestations can therefore easily arise from sleeping on straw or blankets where a lousy individual has slept a few days previously. It is important to remember that fluctuations in temperature retard the development of the eggs and that, even in a temperate climate, eggs on clothing may remain a possible source of infestation for about 25–30 days, which is approximately the limit of life in the egg.

Severe infestations readily occur in those who have to wear their clothes continuously. It should be noted that lice tend to leave their host if he has a fever or if his temperature falls at death, and thereby epidemics of louse-borne diseases may occur.

Examination for lice.—Persons harbouring body lice usually have scratch marks scattered on the body, particularly on the shoulders and waist. The actual bites of the insect may be seen as tiny punctures with an encircling area of erythema ; the clothes should be carefully searched, particularly the under-garments, with special attention to the seams and folds, for it is here that the eggs will be found. The eggs are the size of a pin's head (0·8 mm. long by 0·3 mm. broad) yellowish white in colour, goblet-shaped, and firmly attached at the lower end to the cloth fibre by a cement secreted by the female at the time of laying.

When making an examination be careful to stand to windward of the clothes and person examined, for it has been shown that lice can be blown from one person to another.

Preventive Measures.—General cleanliness is indicated, and in hot countries the axillæ may with advantage be shaved. It is very necessary to pay attention to blankets, beds, dug-outs, huts, tents and billets, for these may constitute foci of infestation—that is, if they have been used by lousy individuals, for man himself is the sole breeder and active distributor of these parasites.

Reinfestation may occur within thirty minutes if outer clothing is left lousy, or on the first night of using lousy bedding. Bedding, billets, and other quarters should therefore be disinfested while the men themselves are being dealt with at the cleansing and disinfestation centre.

The following are important points which should receive special attention in connection with the prevention of lousiness in troops on field service :—

1. All soldiers should be inspected once a week whenever possible, and at the same time examined for lice and scabies. Unremitting attention is required.

2. Men who are found to be verminous should be disinfested as soon as possible so as to check the evil at the start.

3. All soldiers should receive a bath once a week, the bath being followed by a change of underwear.

4. Where men are prone to become verminous, disinfestation should be practised frequently.

5. Disinfestation should be applied to all men who live in close association, none being allowed to escape the process. Every

article of clothing pertaining to every man, including his cap, greatcoat, blankets, and pack should receive attention. Various articles which are the soldiers' personal property may harbour lice, and, unless such nits and lice are removed, a man may reinfest his clothes.

6. Bathing should be controlled to see that it is efficiently carried out, the men and their clothing being inspected after the bath and before being allowed to dress.

7. The larger the number of men loused at one time the better since there will be fewer verminous companions from whom they may subsequently become reinfested.

8. As far as circumstances will permit, the cleaned men should be kept apart from the uncleaned.

9. Soldiers proceeding to the battle zone or returning thence should in either case be examined before they are allowed to mix with other men. A single lousy individual may infest others with whom he associates.

10. The hair should always be cropped short, especially at the sides and back of the head.

11. The personnel employed in lousing should be permanent, especially instructed, and trustworthy, to ensure efficiency and continuity in the established methods of treatment.

12. This personnel should have unlimited facilities for bathing, be subject to inspection and control once a week, and keep their hair close cropped. They should wear protective clothing whilst engaged in their duties, and should be employed either on the clean or unclean side of the establishment at one time only.

13. Clean or disinfested effects should not be stored, even temporarily, where infested articles have been kept. Such effects should be kept rigidly apart.

14. Carts and transport wagons for the conveyance of infested articles are not to be employed for the transport of clean effects without previously being disinfested.

15. It should be noted that the most reliable means of destroying lice and nits are hot air or steam.

16. It should be represented to those in authority that disinfestation cannot lead to the removal of dead nits from the clothing, to the fabric of which they are firmly cemented by the mother insect, and so they have to be removed mechanically with the edge of a knife or finger nail. This operation can be performed by the soldier himself.

Methods of Destruction of Lice.—The most satisfactory methods of destruction available are dry heat (hot air) or moist heat (steam).

1. *Dry Heat.*—Lice and their nits are killed by exposure to a temperature of 55° C.–60° C. for ten minutes, or to 70° C. for one minute. Various means of applying dry heat to clothing and equipment exist and may be of an improvised type such as the

employment of flat irons or of a more specialized type such as the Millbank portable hot air disinfestor and drying machine.

2. *Moist Heat.*—Lice and nits are killed rapidly by exposure to a temperature of 80° C. or over. In practice a temperature of 100° C. is used. Steam disinfestors may be of an improvised type such as the Serbian barrel. Special apparatus for the purpose is also available and varies in size from disinfestors small enough to be carried on mules to a machine such as the A.S.H. steam apparatus carried on a 30-cwt. lorry.

A jet of steam played on the seams of clothing and the like is effective and is a simple means of applying moist heat which may be useful at times in the absence of more specialized apparatus.

As a palliative and preventive measure N.C.I. powder (naphthalene 96 per cent., creosote 2 per cent., iodoform 2 per cent.) applied to clothing is of value. A.L. 63 is more effective; it should be rubbed into the seams of all the clothing worn next the body, and a small amount may be put into the socks. ¾ oz. of A.L. 63 should be used in a single application which should be repeated once every seven or nine days. Anti-louse belts are also employed. They are made of cotton sewn into pleats to attract lice and impregnated with a chemical fatal to these insects. The belt is worn next the skin; dead insects are removed daily; and after a month it is washed and re-impregnated. Unfortunately these belts often irritate fair skins, but they may be useful for native labourers.

Finally, infested materials may be dealt with by soaking in 2½ per cent. cresol for sixty minutes at any temperature above 50° F.

For the mass cleansing of men such as native labouring gangs prior to enlistment and the like a useful dip is the following:—Liquor cresoli saponatus fortis 2½ parts, paraffin 1 part, soft soap 2 parts, N.C.I. powder ½ part, water 94 parts.

Lice beneath bandages which cannot be removed may be treated by application of naphthalene, eucalyptus oil, or oil of turpentine.

It must be remembered that lice frequently "sham dead" and that the only reliable sign of death is when they shrivel and become brittle. Eggs killed by dry heat shrivel and collapse, and when killed by moist heat they become dull and opaque.

Pediculus humanus capitis.

In almost all points of its life-history this parasite resembles the body louse.

Although usually confined to the head, *P. humanus capitis* (Fig. 3, *a*) may spread all over the body, infesting other hairy parts. Nuttall describes a case of infestation with head lice limited to the pubic hair.

Examination for Head Lice.—The head of the suspected person should be carefully examined for the actual parasites or their eggs. The latter—popularly known as "nits"—are minute yellowish-white, goblet-shaped bodies, and are found firmly cemented to individual hairs.

It must be emphasized that a recently-acquired infestation with head lice may be missed if the head is not gone over carefully with a fine-tooth comb. A search made with an ordinary brush and

comb cannot be relied on. Later, when the eggs have been carried away from the scalp by the growth of the hair, an infestation previously indiscernible may become distressingly apparent.

Preventive Measures.—The best safeguard from infestation is to wear the hair cropped close and to wash the head frequently with carbolic soap or cresol soap solution (Jeyes' fluid 1½ oz., soft soap 1½ lb., water 10 gallons.)

Destruction of Head Lice.—The heads of infested persons should be thoroughly combed and treated with a suitable local application. Carbolic acid (1 in 40) is valuable, the hair being thoroughly saturated with the solution. It is then lightly squeezed, tied up in a towel for two hours, and then washed. Nits as well as lice are killed by this means.

Equal parts of kerosene and olive oil applied for twenty-four hours may be used in a similar manner, while a modification of the paraffin method in which an emulsion of the following composition is employed is said to be even more valuable :—

Kerosene 74 per cent.
Arachis oil 20 per cent.
Tar oil 5 per cent.
Oil of lemon grass 1 per cent.

Soaking the hair thoroughly with a mixture of 7 parts methylated spirit and 3 parts of water is effective. Xylol 25 per cent. in vaseline and lanoline can also be recommended. If the scalp is much inflamed emollient ointments are preferable, such as mild preparations of white precipitate ointment or the yellow oxide of mercury. Thorough washing of the scalp after treatment should be carried out with cresol soap solution or carbolic soap.

Ten per cent. acetic acid or vinegar, especially if warm, is useful for loosening the nits from the hair prior to washing or combing the head.

Phthirus pubis

Phthirus pubis usually infests the hairs of the pubic and perianal regions, but inspection should not be limited to these areas. It is frequently found in the axillæ, the inner and back part of the thighs, even as far as the knees in hirsute individuals, on hairs on the lower abdomen, around the nipples and occasionally on the eyebrows and eyelashes ; even the head may be invaded. (*P. pubis* is the only louse that infests the eyelashes). It is a much flattened creature, and the leg claws are particularly strongly developed, giving it the appearance that has led to its popular name (Fig. 3, *c*). It is much less mobile than *Pediculus*, and does not, as far as is known, transmit any disease.

Examination for *P. pubis*.—Infestation by this parasite causes intense irritation, and the bites being confined to a limited area may lead to inflammation accentuated by scratching and, if the eyelashes are involved, to a marginal blepharitis. The presence of the parasites can be ascertained in the same manner as that adopted for *P. humanus capitis*. In addition, look for the pale, bluish-grey maculæ (maculæ ceruleæ) on the skin which, if present, are characteristic of *Phthirus* infestation. The louse itself is almost transparent,

and very close inspection may be required for its discovery. The nits are more easily seen than the adult insect.

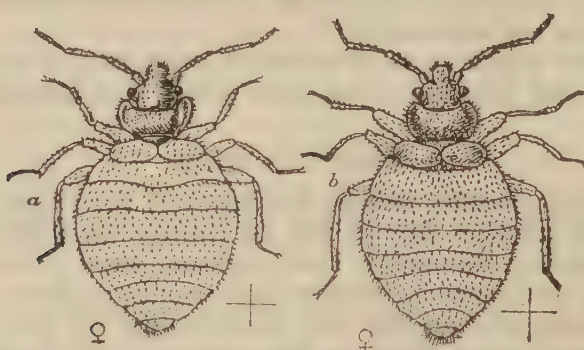
Destruction of *P. pubis*.—Thorough cleansing with soap and water is the first essential, followed by the application of a perchloride of mercury (1 in 1,000) lotion in equal parts of alcohol and water, or in water to which a small amount of vinegar or acetic acid has been added. Mercurial ointments, especially the official yellow oxide or ammoniated mercurial preparations, are efficient but are not pleasant to use and may at times lead to dermatitis. Two or three applications at daily intervals of xylol 20 c.cm. in 30 grammes of vaseline freshly prepared are effective. Inspection after treatment is essential, particularly of the perianal region and backs of thighs as treatment of these areas by attendants is frequently omitted. Unless the medical officer has facilities for supervising personally the treatment and progress of the case, the areas should be shaved before the remedies are applied.

For infestation of the eyelashes and eyebrows vaseline and yellow precipitate (1 in 50) are specially recommended

THE BED-BUG

Two species of bed-bug are important, *Cimex lectularius* and *C. hemiptera* (=*rotundatus*) (Fig. 4, *a* and *b*). The former is the common bed-bug of northern latitudes, the latter the bed-bug of the tropics. Both have much the same habits and life-history.

Fig. 4.



a. Cimex lectularius, the common bed-bug of the temperate zone.
b. Cimex hemiptera, the bed-bug of the tropics.

Diseases transmitted by.—None definitely known, but the bed-bug has been accused of carrying kala-azar, plague, anthrax, relapsing fever and typhus. It is an efficient experimental host of *Trypanosoma cruzi* and *Leptospira icterohæmorrhagiæ*.

Cimex lectularius *and* C. hemiptera

Both males and females suck blood, and they are nocturnal in their activities. During the day-time they usually hide in cracks in floors, walls and furniture, or in beds, among the folds of the sheets and blankets, in or below the mattress, or, in fact, anywhere where

they may remain quiet and obscure until the night. Bed-bugs are capable of migration from house to house or from tent to tent and can live for long periods—nine months or more—without food, so that an infested place may remain so for a lengthy period. They are sensitive to temperature and are apparently more numerous in cold than in hot climates. It is remarkable how very few bed-bugs are found in Mesopotamia. A temperature of 96° F. to 100° F., with a fairly high degree of humidity, is said to kill large numbers. Adult bugs can resist temperatures below freezing for some considerable time. Eggs and larvæ are not quite so hardy.

The female lays a large number of eggs, which are deposited in clusters of twenty or more, adhering together because of a gelatinous substance with which they are covered.

A single *C. lectularius* in captivity has been known to lay as many as 111 eggs in eighty-one days. There is no special season for egg-laying, and it continues throughout the year, the eggs being deposited in the hiding-places of the adults.

The eggs are a dirty white colour, about 1 mm. in length and ovoid in shape, the upper end having a disc-shaped cap (operculum that projects more over one side than the other. The larvæ hatch out in from four to nine days, and feed soon afterwards if a blood meal is available. Four or five days thereafter the larvæ moult and attain the first nymphal condition, and after four subsequent moults the adult stage is reached in about six or seven weeks from the hatching of the egg. Sexual maturity is attained from ten days to a fortnight later. In an unfavourable environment the period of development may be much prolonged.

Examination for Bed-Bugs.—The walls, floors, ceilings and the contained furniture—particularly wooden beds and bedding—of suspected rooms should be carefully examined, especially obscure corners and cracks in the walls, etc., that are likely to prove hiding-places for the parasites. In the case of beds and bedding, special attention should be devoted to folds in the mattress and to the crevices formed at the junction of the bedstead units.

Preventive Measures.—Cleanliness is the best safeguard, accompanied by the removal of all possible hiding places for the insects. Cracks in the walls, etc., of houses should be filled in ; picture rails, other woodwork and wallpaper may have to be removed, walls and ceilings distempered and repaired, and woodwork replaced.

Bedsteads may be treated with paraffin, either in the form of a spray, or by applying it with a rag. Vaseline may be used similarly. The application of tanglefoot (*see* p. 43) to the legs of bedsteads is also a valuable preventive.

Destruction of Bed-Bugs.—Fumigation by hydrocyanic acid gas is largely used, but the method is dangerous, expensive, and difficult to carry out. Its use is justifiable in permanent barracks or hospitals when badly infested, the work usually being placed in the hands of civilian firms with special experience.

Good results are reported from fumigation with heavy naphtha, and this method has in some places largely replaced the first named. Fumigation with sulphur dioxide obtained by the combustion of sulphur is a safe and comparatively simple method to employ,

using 6–7 lb. of sulphur to fumigate 1,000 cubic feet, but is not as effective as hydrocyanic acid gas or heavy naphtha.

Fumigation with formaldehyde gas gives fairly good results, but it is a method which is more applicable to the smaller type of room with a comparatively low ceiling.

A paraffin or benzine blowlamp may be used to kill the adults and their eggs in their hiding places. The lamp should be pumped up to a strong blast and the flame directed against and rapidly moved over all the suspected places. In this way a temperature lethal to bugs and their eggs is produced, but with the lamp moving rapidly the heat is not sufficient to injure the walls or woodwork. This method is particularly useful when iron bedsteads are used.

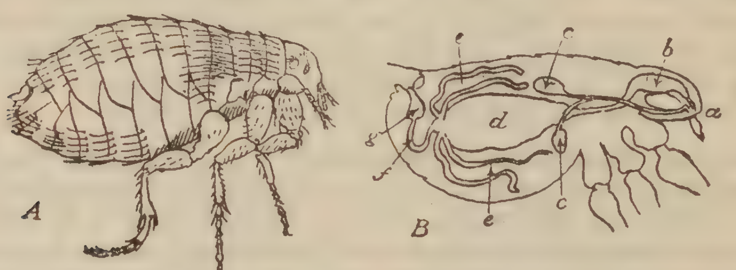
A temperature of 160° F. continued for ten hours has been found to kill the bug in all its stages. Boiling is of course effective but of limited application.

Spraying methods are of some value in small houses but should be repeated at frequent intervals. The best agents to employ are formalin, petrol, toluene, or the following crude oil emulsion :—Soap, 3 parts, dissolved in hot water, 15 parts, to which while still hot kerosene, 7 parts, are gradually added with vigorous stirring.

FLEAS

Diseases transmitted by.—Plague ; the varieties of helminthiasis caused by the trematodes *Hymenolepis diminuta* and *Dipylidium caninum* ; also murine typhus, transmitted from rat to man by the rat flea, *Xenopsylla cheopis*.

Fig. 5.—*A*. The Human Flea, *Pulex irritans* : *B*. Internal anatomy of same.



a Proboscis ; *b*. Sucking pharynx ; *c*. Salivary glands ; *d*. Stomach *e*. Malpighian tubules ; *f*. Intestine ; *g*. Rectum.

Pulex irritans (Fig. 5) is the only flea of which man is the normal host, but fleas of many species may attack him on occasion. The most important of these is *Xenopsylla cheopis*, though this is by no means the only flea which may convey plague to man. The following fleas are proven to carry plague and have been found on rats. With the exception of *C. agyrtes* they are all known to bite man. The normal hosts and the distribution are given in brackets : *Xenopsylla cheopis* (rats ; hot countries, Egypt, India, on shipping and in sheds in docks and in ports). *X. astia* (rats ; Asia). *Ceratophyllus fasciatus* (rats ; Europe, Egypt). *Stivalius ahalæ* (rats ; S.E. Asia,

China, Japan, etc.). *Ctenophthalmus agyrtes* (field mice; Europe . *Hoplopsyllus anomalus* (squirrel; U.S.A.). *Leptopsylla musculi* (mouse; Europe, Asia, Africa). *Ctenocephalus canis, C. felis* (dog and cat; Europe, Asia, etc.). *Pulex irritans* (man; world-wide). (*See also* Plague.)

The female lays large eggs, singly, and these are not attached to the residential host, but, when laid, fall to the ground. They are found most readily in the sleeping-places of animals, and can be readily seen by the naked eye. In summer the eggs hatch in from two to four days, but in winter the incubation period may be extended to a fortnight.

The eggs hatch and an active, footless larva emerges, dirty white in colour and sparsely clothed with long, fine hairs. It lives among dust, on floors, etc., feeding on organic matter. The larva attains its full development in about two weeks when the weather is warm, then seeks a quiet place and spins a cocoon, in which it pupates. The pupal stage extends over a period of about another fortnight, and the adult flea emerges.

These usual periods are subject to considerable variations. For instance, in the case of *X. cheopis*, Bacot showed that the larval stage might last from twelve to eighty-four days, and the cocoon stage from seven to one hundred and eighty-two days.

Adult fleas are, as a rule, only too much in evidence, but in order to find the immature stages, the dust from the floors of the suspected place should be brushed up and examined with a hand lens for the eggs, larvæ and pupæ described above.

Preventive Measures.—Hard materials should be used for floors. No dust or fine organic material should be allowed to accumulate, and wherever possible, textile floor coverings should be dispensed with. Floors may be sprinkled with powdered naphthalene or other deterrent powders. Such powders can also be applied to the clothes as a preventive measure.

Control of the animal hosts of the insects is essential and the disinfestation of domestic animals at frequent intervals is necessary. Rats and mice should be kept down and attention paid to hen-houses and the like.

Washing down of rooms, etc., with chlorinated lime wash is a useful preventive measure.

Destruction of Fleas.—Where the nature of the building allows of it, the burning on the floor of patai (dried grass) to a depth of 4 inches will give a two-foot flame and destroy fleas.

There are various disinfectant emulsions which, poured into cracks and crevices, give good results. Of these the most important are the following :—

(1) Cresol 5 parts.
Soft soap 20 parts. } added gradually to 75 parts of hot water.

(2) Kerosene 20 parts.
Soft soap 1 part.
Water 5 parts.

The soap is added to the water and the kerosene is then stirred in. The mixture is known as pesterine.

Naphthalene dissolved in benzine and used for the treatment of cracks and crevices is valuable, while spraying with a pyrethrum-kerosene spray will give good results. The mixture should contain pyrethrum ½ lb. in kerosene 1 gallon.

Fumigation with sulphur dioxide may be employed, as also with hydrocyanic acid gas or cresol vapour. Fleas in rat burrows leading from houses may, however, escape.

It is claimed that "neem-batti" kills rats and fleas within five minutes and is altogether more effective than the ordinary fumigation of houses. It is prepared and used as follows :—Potassium chlorate 2 drachms, potassium nitrate 1½ drachms, sulphur 2 drachms are powdered and mixed with 5 drachms of mustard or castor oil to make a paste, to which 1 drachm of red pepper and a handful of crushed and dried neem leaves are added. This is placed in a rat hole over a 9-inch wick of cloth soaked in a saturated solution of potassium nitrate, thoroughly dried and ignited, the holes being closed.

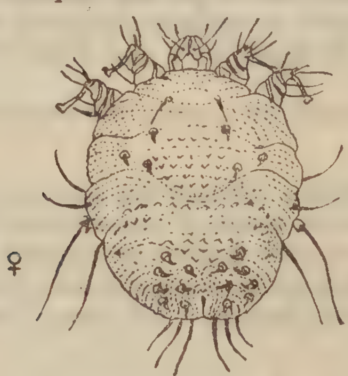
The potent effect of sunlight in the destruction of fleas should not be lost sight of.

Fleas may readily be trapped with sticky paper and other devices, but these only operate on a small scale. A bed may be protected by placing a zone of sticky paper 13 inches wide on the floor round it so long as the fleas are not breeding inside the zone. Persons entering plague-infected houses should make their clothing as flea-proof as possible by means of puttees, gloves, etc.

THE ITCH MITE

Sarcoptes scabiei, the cause of "the itch," is invariably a nuisance to armies in the field, chiefly because of the pyodermic infections which usually complicate untreated scabies.

Fig. 6.—*Sarcoptes scabiei*. The "Itch Mite."



Female mite

The female mite (Fig. 6) can crawl at a speed of up to 2 cm. per minute and infestation usually occurs during a period of close bodily contact. Infestation via fomites can occur.

The fertilized female moves over the skin until she finds a site suitable for burrowing; she appears to prefer an area where the

skin may at times be lax and small folds may be formed. The sites of election are the webs between the fingers, the fronts of the wrists, the extensor surfaces of the elbows, the anterior axillary folds, the edge of the navel, the buttocks and the penis. In about 60 per cent. of cases the site of the original infestation is the upper limb. The mite burrows in the horny layer, the rate of burrowing varying between 0·5 and 4·5 millimetres per day. She does not voluntarily leave her burrow, but lays her eggs there at the rate or two or three every twenty-four hours until some 40 or 50 have been laid, and dies after six or seven weeks. Larvæ emerge from the eggs. The life cycle may be summarized as follows :—

Egg stage	2½ days or more.
Larval stage	1½ to 3 days.
Nymphal stage	1½ to 2½ days.
Immature female	2 to 4 days.

The nymphal stage is terminated by a moult, when either an adult male or an immature female is formed. The latter has to moult once again to produce an adult female. The shortest period which elapses from the deposition of the egg to the emergence of the adult female may be less than eight days.

The larvæ leave the parent burrow, crawl over the skin and make small peri-follicular burrows. The nymphs also make little burrows and the males lie either on the surface or in small " pockets " in the epidermis. Probably it is only the adult oviparous female which makes the classical burrow. On an average not more than 10 to 15 adult female mites are found on an infested person, for there is much wastage of life, ova may be infertile, and larvæ and nymphs die before reaching maturity.

Itching does not occur until the infested person becomes sensitized to some substance (the saliva ?) produced by the mite ; the development of this sensitization may be delayed, which is why some patients with scabies say that they do not itch. Conversely, in some persons, itching may occur at the site of a burrow, although the patient has been treated and is known to be cured ; the assessment of post-scabietic pruritus may be difficult and entails the dissection of any residual lesions with a histological needle and examination of the lesions and their contents under a low-power microscope lens.

Treatment.—Many drugs, *e.g.* mercury, beta-naphthol, balsam of Peru, Styrax, Rotenone, etc., will cure the disease if properly applied.

Two methods of treatment are recommended :

Benzyl benzoate.—Of many formulæ which have been suggested the following are of importance :—

1.	Benzyl benzoate	33⅓ per cent.
	Soft soap	33⅓ ,,
	Spirit, mineralized, methylated ...	33⅓ ,,
2.	Benzyl benzoate	20–25 ,,
	Spirit, mineralized, methylated ...	75–80 ,,
3.	Benzyl benzoate	25 ,,
	Lanette wax	2 ,,
	Water	73 ,,

The patient is given a hot bath (temperature about 103° F.). While bathing he is thoroughly rubbed down with soft soap, using a nailbrush to break open the burrows and expose the *Sarcoptes* and her ova. He occupies the bath for at least ten minutes. On leaving the bath he dries himself; then the lotion or emulsion of benzyl benzoate is applied with a brush from the neck to the feet. The lotion is allowed to dry and a second application is made. The patient must not wash for twenty-four hours, when a second bath is given and another application of the benzyl benzoate is made. Eight to twelve hours later a final cleansing bath is given, and unless there are septic complications, the patient is fit for discharge.

Under conditions of active warfare benzyl benzoate lotion (without soap) or emulsion may be applied without any preceding bath. Two applications should be given within half an hour and the patient should then put on his clothes and return to duty. He should not wash for twenty-four hours. If during this time his hands and wrists become filthy they may be washed provided they are re-painted immediately with benzyl benzoate. Twenty-four hours after the first application the same treatment is repeated. On the following day the patient should have a bath, or should wash from neck to feet with water from a bucket. He should report to the medical officer once a week for six weeks to ensure that he is cured. If it is found at the first medical inspection (seven days after the treatment) that a patient is not cured, a second application of benzyl benzoate should be made. If the infection persists the patient should be referred to a specialist in dermatology.

Sulphur Ointment.—The preliminary bath, with soaping and scrubbing, is given ; when the patient has dried himself 2 ounces of ung. sulphuris are rubbed thoroughly into the skin from the neck to the feet, twenty minutes being taken for this procedure. The routine should be repeated twice at intervals of twelve to twenty-four hours (*i.e.* three inunctions with sulphur ointment in all). The patient should be kept warm, as the therapeutic effect of the ointment is thereby increased, and in temperate climates it is best to keep him in bed.

Blonde persons, particularly those with red hair, develop sulphur dermatitis easily, and for these it is advisable to dilute the ointment by adding 1 part of soft paraffin or zinc ointment to 2 parts of sulphur ointment.

General.—While the patient is under treatment his clothing and bedding should be disinfested, except under conditions of active warfare.

After receiving treatment for scabies, the patients should have a weekly skin inspection for a month. Contacts of cases should be kept under observation, since early diagnosis and treatment will prevent the spread of infection.

Prevention.—The importance of adequate ablution and bathing facilities cannot be over-emphasized, as also of satisfactory laundry arrangements for undergarments. The communal use of articles of clothing, such as sports clothing and the like, should be discouraged, whilst special care must be taken to ensure that blankets are marked in the usual way, in order to avoid the accidental transfer of one man's blanket to another.

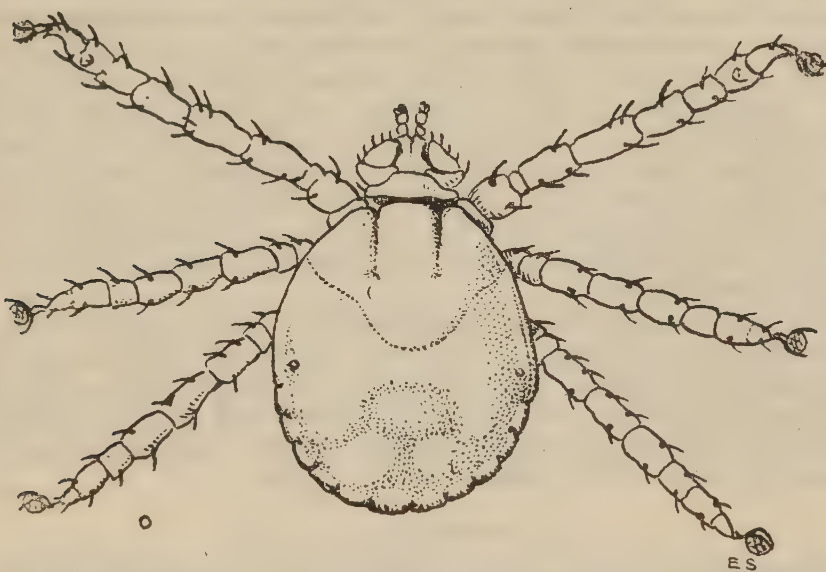
Contacts of cases should be kept under observation.

A considerable aid in suppression amongst units is fearless reporting and the publication of incidence curves and tables.

TICKS

These arachnids are usually divided into two families—Ixodidæ, hard ticks, and Argasidæ (more correctly, Argantidæ), soft ticks. Some zoologists do not give familial rank to these groups and regard them as subfamilies only. Amongst ticks the Ixodidæ can easily be recognized by their terminal projecting mouth parts, and by the presence of a dorsal shield which is small in the female and in the male covers practically the whole body. The mouth parts of the Argasidæ are not terminal, consequently they are not seen in a dorsal view. There is no dorsal shield in either sex.

Fig. 7.



Tick larva. (After Castellani and Chalmers.)

From the tick egg minute larvæ with only three pairs of legs emerge. The larvæ of Ixodidæ (Fig. 7) await on grass, etc., the passing of a suitable host to which they attach themselves. After gorging they drop to the ground, moult, and become nymphs. These resemble the adult in having four pairs of legs but lack genital organs. Similarly the nymphs attach themselves to a host, and after dropping off, moult and become adults. Ticks requiring three individual hosts for their development are often known as three-host ticks. There are also two-host and one-host ticks.

Though the Ixodidæ are of the utmost importance in veterinary medicine, they are known to be responsible for only a few infections of man, such as Rocky Mountain spotted fever,* a typhus-like disease spread by *Dermacentor andersoni*, and fièvre boutonneuse

---

* Another typhus-like disease occurring in India has been attributed to the bite of some tick, but the indictment remains to be established.

spread by *Rhipicephalus sanguineus*, the dog tick. These hard ticks may cause a form of acute ascending paralysis which, especially in children, may end fatally. It appears to be an intoxication due to the injection of the tick saliva during a period of several days' attachment. Recovery is usually rapid if the tick is removed before the muscles of respiration are affected.

Louping ill, an encephalomyelitis of sheep, common in certain parts of Scotland, is due to a virus said to be transmitted by a hard tick, *Ixodes ricinus*. Human infections, especially amongst shepherds, may occur.

When force is used in an attempt to remove an attached tick, one of two things happens—either the surrounding skin is unnecessarily torn, or, as is most probable, the body of the tick comes away leaving the mouth parts buried in the skin. This sets up severe irritation, and may even lead to septic infection ; therefore, rather than forcible removal, the following course is advocated where time permits.

A small camel-hair brush should be dipped in turpentine, benzine, petrol or paraffin and applied between the skin and the under surface of the tick. After a few moments the tick will let go its hold, being killed by the application, and may be swept from the skin with the brush. Any oil may be used for the same purpose, and vaseline smeared over the tick and surrounding skin is equally efficacious. To remove a rostrum that remains in the skin after a tick has been forcibly removed, cocaine should be applied to the spot and the rostrum extracted with needle forceps, and the wound treated antiseptically.

The Argasidæ in their feeding habits usually resemble bed-bugs rather than typical ticks. They hide during the day, and by night sally forth, and having fed return to their lairs again. The most important member of this family is *Ornithodorus moubata*, which is a host of the organism causing Central African relapsing fever. It is necessary to say a little regarding this vector.

Ornithodorus moubata

This blind tick, the general appearance of which is well shown in Plate 2, is a greenish-brown colour when alive, and, like all the Argasidæ, does not possess a shield or scutum, but is covered by a leathery integument. This integument is dotted over with close-set granules and exhibits several grooves both on the dorsal and ventral surfaces. In gorged females these disappear. Important diagnostic characters are : the broad rounded anterior extremity, the absence of a deep, waist-like constriction, the distinct tubercles on the distal segments of the legs, and the absence of eyes.

Unfed adults are about 4/10ths of an inch in length, but a gorged female may be well over half an inch long and be very nearly of an equal breadth. *O. moubata* lives in native huts and in rest-houses which natives may have occupied. It is commonest along trade, travel and caravan routes. During the day it hides in cracks and crannies in the walls and floors, or about the bases of the vertical wooden roof supports, or in the thatched roofs, or more rarely in cracks in native wooden bedsteads. At night it sallies forth on the blood quest. It feeds both on man and animals, and engorgement

takes from a few minutes to about two hours, according to the stage of the tick. The bite is painful and may leave a tingling sensation behind it. The fecundated female, after a meal of blood, lays from 50 to 100 nearly spherical, glistening, golden-yellow eggs in batches, the number in each batch varying. The eggs, which are agglutinated into masses, are laid in the soil or in other hiding places. They hatch in about twenty days, and as the hexapod larval stage is practically suppressed it is an eight-legged nymph which emerges from the egg-shell and the larval skin. Sometimes, however, the larvæ are free living.

There are three or four nymphal stages, and these, as well as the adults, may attack man. The adult may live for several years, and may exist for long periods unfed—in one instance, cited by Warburton, for so long as five years. The offspring of an infected tick are themselves infective to at least the third generation.

The bites are best treated by bathing the bitten part in very hot water and applying a strong solution of bicarbonate of soda. If itchiness persists, smear with a menthol vaseline. For other points, including prophylaxis, *see* Relapsing Fever (p. 214).

O. savignyi, a closely allied species, has been proved capable of conveying relapsing fever, and appears responsible for the spread of the disease in Somaliland and Abyssinia. This tick differs from *O. moubata* in possessing two pairs of eyes, of which the posterior pair are the more easily seen. One of these lies on either side of the body in the space between the 2nd and 3rd pair of legs, and appears as a slightly raised, reddish dot. The beginner must beware of mistaking the much larger breathing spiracle for the eye. The hind tarsus of *O. savignyi* is longer than that of *O. moubata*, and for this reason the terminal tubercle in the former species appears very remote from the two preceding tubercles. This character will readily be appreciated if the hind tarsi of these two species are compared. For other tick vectors of spirochætes, *see* Relapsing Fever.

ANTS

As regards this group it need only be remarked that ants have been incriminated experimentally in the spread of typhoid and cholera and emphasis should be laid on the fact that food must be protected from their predations. Ants may travel from infective material to foodstuffs, carrying with them pathogenic organisms and making it essential that food be placed out of their reach. This is especially important when cholera is present.

Ants may be kept from food on tables by tying paraffin-soaked rags round the legs of the latter. Kill the insects by the use of insect powders, such as borax.

If an infestation of ants occurs it is usually the larder that is raided. If the place of entry into the house can be traced, a small sponge soaked in sweetened water, placed near the entrance, will attract the ants and when the pores of the sponge are filled with them, it may be dropped in boiling water and the process repeated. To avoid the incursions of the insects, all food scraps should be destroyed, stores carefully protected, and paths of entry noted. The latter should be blocked up as far as possible and sprayed with kerosene

oil and powdered with borax. The nest should be traced by the "ant route" and destroyed. The most effective means of doing this is by pouring about two tablespoons of carbon bisulphide down the entry to the nest and covering with earth.

Nests may also be destroyed by digging up the earth over and around them for several inches, pouring in about a pint of petrol or kerosene and setting it alight. Boiling water poured repeatedly into the nests is also useful. If the nest cannot be located, jam jars lightly coated inside with treacle may be placed at suitable points in the ants' runs. The worker ants are trapped in the jars in large numbers, and after a time the nest becomes so denuded that the queen ant either dies of starvation or moves her quarters, with the few remaining workers, to a safer place.

COCKROACHES

To keep rid of these pests, floors should be swept and other feeding grounds kept as clear as possible of food debris. Pyrethrum powder or borax mixed with a little sugar sprinkled on the floor near sinks, stoves, fireplaces, and crevices each night for several weeks will effect a material reduction in numbers. Complete eradication is always difficult. Baits of poisoned food, such as sodium fluoride mixed with some soft food, may be of assistance. Poisonous powders are more frequently used, of which the best has the following composition:—sodium fluoride 3 parts, fresh pyrethrum powder 1 part, plaster of paris 1 part, sugar 2 parts. Breeding places should be tracked down and cracks filled in or flooded with boiling water, formalin, or other liquid poison. Fumigation with sulphur dioxide and the like will deal fairly efficiently with nymphs and adults, but is unlikely to reach the eggs, which are protected by a specially hardened case. Care must be taken not to contaminate food with any poisons used.

WINGED PESTS

Under this heading Mosquitoes, Sandflies, Midges, House Flies, Stable Flies, Tsetse Flies, the Congo Floor-maggot Fly, Carcase Flies and Hippobosca are included.

MOSQUITOES

Diseases transmitted by.—Malaria, dengue fever, yellow fever, filariasis, Rift Valley fever.

Mosquitoes constitute the family, Culicidæ, and are distinguished by the venation and scaling of the wing. The second, fourth and fifth longitudinal veins are forked (Fig. 8), and there are always scales on the hind margin of the wing. The Culicidæ are divided into two subfamilies: (1) Culicinæ, which have a very long proboscis, and scales on the longitudinal veins; and (2) Corethrinæ, which possess only a tiny proboscis, and have hairs on the longitudinal veins. These latter do not bite and are of no medical interest.

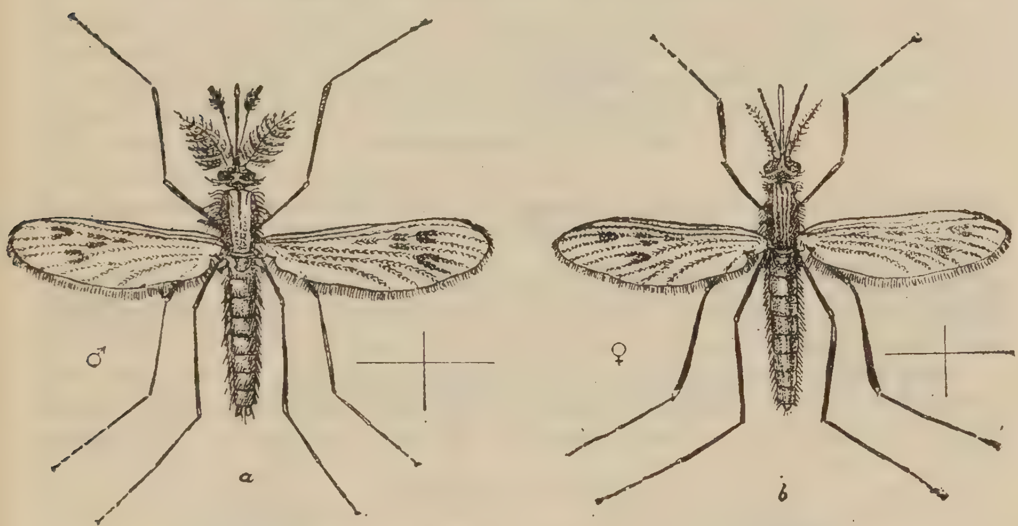
In the sub-family, Culicinæ, four tribes are generally recognized —Anophelini, Culicini, Megarhinini and Sabethini. The first two include all the known disease carriers, and are considered

hereafter. The Megarhinini are large non-biting mosquitoes with a proboscis recurved on itself like a pot-hook. The Sabethini are small jungle mosquitoes which are not concerned in the spread of any disease.*

ANOPHELINI

This tribe may be regarded as comprising one genus only, *Anopheles*, which includes all the known carriers of malaria. The sex of anophelines, and of the vast majority of culicines, may be recognized by the densely haired and plume-like antennæ of the male, those of the female being very sparsely haired (Fig. 8). Female *Anopheles* may be identified by their palpi which are as long, or almost as long, as the proboscis, whereas those of female culicines are always distinctly shorter than the proboscis, and are often minute. While it is true that the wings of anophelines are more often spotted than

Fig. 8.—*Anopheles maculipennis.*



a. Male. **b.** Female.
Note the scutellum, a raised bar crossing the thorax at about the level of the attachment of the wings.

those of culicines, reliance must not be placed on this difference, for some anophelines have clear wings, and a few culicines have their wings markedly spotted. The resting attitude often serves to distinguish these two tribes, culicines resting parallel to the surface, while anophelines appear to "stand on their heads" (Fig. 9). It should be noted, however, that all species of *Anopheles* do not assume this position.

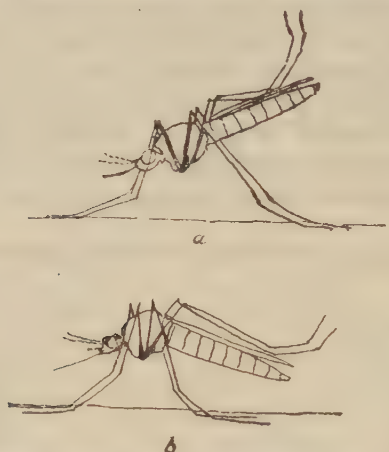
Important diagnostic characters of *Anopheles* are: (1) Palpi long in both sexes, clubbed terminally in the male. (2) The scutellum is simple, *i.e.* the posterior margin is not lobed. (3) They are the least scaly of mosquitoes and, unlike all others, they never have the abdomen covered with a complete smooth coat of scales.

The female alone sucks blood, and after a meal she seeks a quiet

* There is some experimental evidence to suggest that certain sabethine mosquitoes may act as potential vectors of jungle yellow fever.

place in which she can digest the blood while her eggs rapidly mature in her ovaries. In the course of a few days she makes for water, where she lays her eggs. These are cigar-shaped, and the covering membrane does not fit closely but projects in a variety of shapes to form floats. After a few days the eggs hatch, and minute, active

Fig. 9.—Anophelini (*a*) and Culicini (*b*).

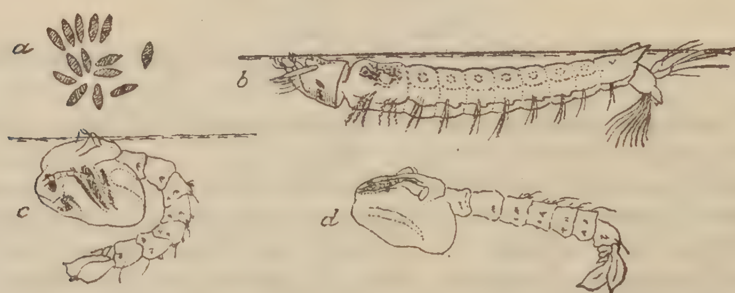


In resting position. Note angles assumed by the bodies of the insects relative to the surface on which they are resting.

larvæ emerge. These are the so-called " wrigglers," or as they might be better termed, " darters," and owing to their transparency and small size they are at first difficult to see.

Anopheline larvæ, unlike all other mosquito larvæ, are not provided with a breathing tube or syphon. Being surface feeders they lie just below, and parallel to, the surface of the water

Fig. 10.—*Anopheles.*



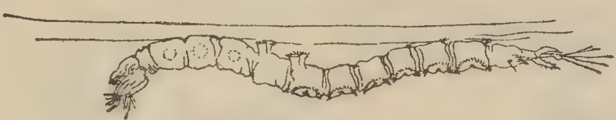
***a.* Eggs ; *b.* Larva(note resting position, body *parallel* to surface of water) ; *c.* Pupa *d.* Empty puparium from which mosquito has emerged.**

(Fig. 10, *b*). The vast majority of culicine larvæ rest with their bodies at an angle to the surface, hanging suspended by the syphon (Fig. 13, *b*). The larvæ of *Dixa* (Fig. 11), and some other aquatic larvæ, are sometimes confused with those of mosquitoes. If it is borne in mind that mosquito larvæ have a distinctly formed thorax, such a mistake cannot occur.

The larvæ feed and grow rapidly, undergoing four moults. The

time spent in the larval condition depends partly on the temperature of the water and partly on the food supply, but with both favourable this condition is passed through in about a week or ten days. The fully grown larva then casts its skin and attains the pupal condition, when in shape it appears like an overgrown comma (Fig. 10, *c*). The pupa swims by active strokes of its tail and at rest lies just below the surface, breathing through two small tubes or so-called "trumpets,"

Fig. 11.—Larva of *Dixa*.



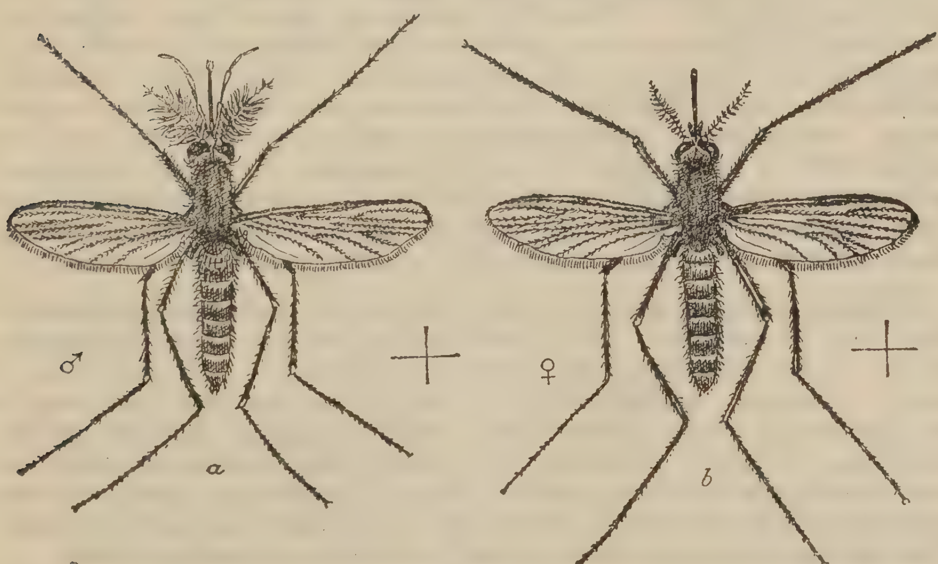
that are situated at the sides of the head and just break the surface film. The pupal stage lasts about a week, and then the pupal case (Fig. 10, *d*) splits and the perfect insect emerges. Anophelines can travel much greater distances than was formerly supposed. With a favouring wind they will traverse several miles, especially if there are suitable resting places *en route*. Space does not permit any lengthier consideration of the bionomics of mosquitoes.

For the carriers of malaria, *see* p. 142.

Culicini

In the Culicini are included the mosquitoes responsible for the transmission of yellow fever, dengue, and the form of filariasis due to *Wuchereria bancrofti*.

Fig. 12.—Culicini—*Culex fatigans*.



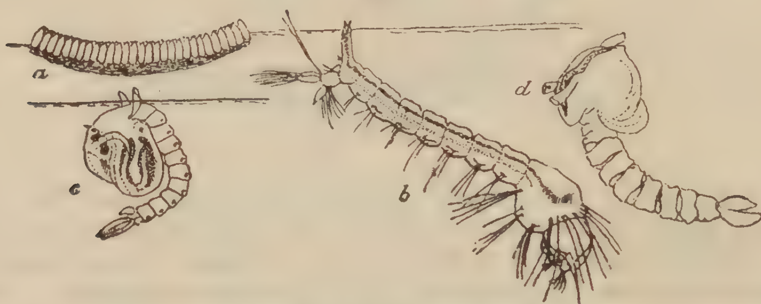
a. Male. *b.* Female.

Important diagnostic characters of the Culicini (Figs. 12 and 13) are: (1) Palpi in the female always distinctly shorter than the proboscis. The male palpi are usually long, but in some cases are short.

(2) The scutellum is lobed. (3) The postscutellum (the smooth area between the scutellum and abdomen) is nearly always bald. (4) The abdomen has a complete coat of scales appressed like those of a fish. As mentioned above, the larvæ are provided with a breathing syphon.

The difficult question of the genera of the Culicini cannot be discussed here.

Fig. 13.—Culicini.



a. Egg raft (side view); *b.* Larva (note resting position, body hanging at an angle from surface); *c.* Pupa; *d.* Empty puparium from which mosquito has emerged.

Yellow Fever.—*Aedes ægypti* has long been regarded as the sole vector of yellow fever. Whilst this remains true for the classical urban yellow fever, recently other mosquito vectors (*Aedes leucocelænus*; *Hæmagogus capricorni*, etc.) have been proved capable of transmitting that variety of the disease known as jungle yellow fever, which is endemic over widespread areas in South America where *Aedes ægypti* does not exist. (*See* p. 283.)

In order to distinguish *A. ægypti* (Fig. 14) from other black and silver mosquitoes, two characters, taken in conjunction, will suffice. These are the absence of any narrow curved scales on the back of the head and the vertex, and the arrangement of the "lyre" marking on the dorsum of the thorax. To determine the first of these, a microscope is necessary. Failing this, the following characters can be noted with a hand lens, or by the unaided eye: the unbanded proboscis; the "lyre" on the thorax; the silver scutellum; the cross bands on the abdomen; and the leg markings—tibiæ entirely dark, hind tarsi with five bands, tarsi of other legs with two bands.

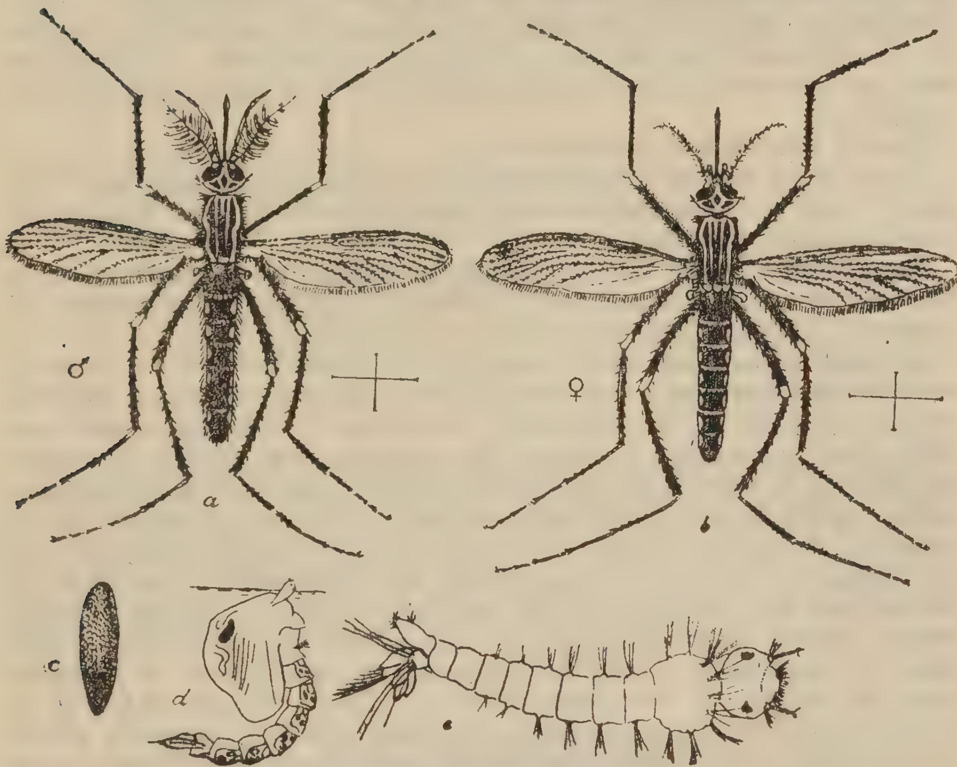
Dengue.—*Aedes ægypti* is also the proved transmitting agent of the virus of dengue. Two other mosquitoes are under grave suspicion, *Aedes albopictus* and *Armigeres obturbans*. *A. albopictus*, a much commoner mosquito than *A. ægypti*, is distinguished from it by the single broad longitudinal stripe replacing the lyre on the thorax. *Armigeres obturbans* is a large black mosquito with no silver markings visible in a dorsal view, but the under surface of the abdomen is silver with a transverse black band on each segment. The proboscis in both sexes is bent, with the convexity dorsal.

Filariasis.—Complete development of the larva of *Wuchereria bancrofti* had been recorded in the following culicines (as well as in three anophelines, *Anopheles subpictus*, *A. gambiæ* and *A. hyrcanus*): *Aedes* (*Stegomyia*) *chemulpænsis*, *Aedes* (*Finlaya*) *togoi*,

A. (*S.*) *variegatus, Culex fatigans, C. pipiens* var. *pallens, C. sinensis, C. tipuliformis, C. tritæniorhynchus, C. whitmorei, Tæniorhynchus* (*Mansonioides*) *africanus*, and *T.* (*M.*) *uniformis.*

Of these *Culex fatigans* and *Aedes variegatus* are the most important insect hosts.

Fig. 14.—Culicini—*Aedes ægypti*=*Stegomyia fasciata.* The "Yellow Fever Mosquito."



a. Male ; *b.* Female ; *c.* Egg ; *d.* Pupa ; *e.* Larva.

Rift Valley Fever.—This somewhat localized disease occurs as a fatal epizootic amongst ewes, lambs and cattle. It is transmitted to man in Kenya, Uganda, the Southern Sudan and some parts of French Sudan and French Equatorial Africa, where it causes a non-fatal dengue-like illness, by a Culicine mosquito, *Tæniorhynchus brevipalpis.*

Control of Mosquitoes

Preventive Measures.—In order to prevent the breeding of mosquitoes all collections of standing water, whether of large size, such as swamps, marshes, ponds and the like, or of small size, such as old tins and other receptacles in which rain water may be trapped, should be eliminated as far as possible. Drainage, filling in, or, in the case of disused receptacles of any kind, removal, are the methods mainly relied on.

If elimination of breeding places is not possible, larvicides, such as kerosene and crude oil, Paris green, or cresol will be necessary, in addition to the removal of aquatic growth.

A useful kerosene-crude oil mixture is the following :—

Kerosene 1 part, heavy oil 2 parts, cresol 1 per cent., the amount required being half an ounce per square yard per week. Malariol, a proprietary preparation now much used, is more effective. Paris green (copper aceto-arsenite) is now widely employed as a larvicide, especially for anopheline larvæ. It is used in a 2–5 per cent. mixture with some light dust, such as road dust, slaked lime, etc., and half to one pound of the chemical per acre is required. Paris green must contain 55 per cent. arsenious oxide and be fine enough to pass through wire gauze of 30 meshes to the inch. Distribution may be effected by hand, by special blowers, or on a large scale by aeroplane.

Cresol, 1 in 50,000 is also effective.

Application of larvicides must be carried out at intervals of 7–10 days. Larvæ-eating fish are sometimes obtainable, but the method is not always satisfactory.

When measures of the above nature cannot be carried out, as in the case of reservoirs and other water storage tanks, screening by means of tightly fitting covers will be required.

As regards running water, everything possible must be done to increase the flow and avoid stagnation. Measures to this end will include clearing of all vegetation, trimming of the edges, and possibly grading, cement lining, or, in certain cases, subsoil drainage. In addition to the above, treatment with the crude oil and kerosene mixture may be necessary, and can be carried out automatically by means of drip cans discharging about twenty drops of the mixture per minute. These are easily made by puncturing a paraffin tin with a nail and inserting a wick of cloth or tow, or by inverting a corked bottle filled with the oil and puncturing the cork. Both kinds of containers should be mounted on some kind of platform over the centre of the water-course. Small streams may be at times treated with larvicides by damming them at suitable points at intervals of 7–10 days, and having in this way brought the water to a standstill, applying the larvicide for a suitable length of time before removing the dams. In irrigated and cultivated country trap pools are often invaluable. They can be made in the soil itself, but it is better to use shallow wooden tubs filled with rain or marsh water. A layer of salt should be sprinkled on the bottom of each tub and some green algæ added in order to make the artificial pools attractive to *Anopheles*. They must be visited at least once every ten days and any larval brood found in them, destroyed. The idea is to make these pools more attractive than any neighbouring potential breeding places. They can often usefully be interposed between a natural mosquito nursery and a camp, village, or town.

Destruction of Mosquitoes.—Trapping is a measure which is easily applied. The usual form of trap is a black wooden box with a movable inside wire gauze cage, and is left, with the end open, in a dark corner of the room, other resting places having been as far as possible removed. The trap is closed at dawn and the inner wire cage with the contained mosquitoes removed and the latter destroyed.

Inside tents, buildings, and dugouts many mosquitoes can be captured by the systematic use of small sweep nets, whilst a goodly

number can also be caught without any contrivance if the hands be well soaped.

Fumigation is of limited application and the use of pyrethrum or sulphur has not been found very practical or satisfactory. The burning of katol oil in barrack rooms and the like in the morning after all doors and windows, except one, have been darkened, with a view to driving out the mosquitoes via the one opened window, has given good results. The mosquitoes may be killed by spraying as they emerge or may be caught in a trap of mosquito netting or "mul-mul" fixed to the window. Good sprays are the following:—

Kerosene (2nd quality) 100 parts.
Oil of wintergreen (crude) 1 part.

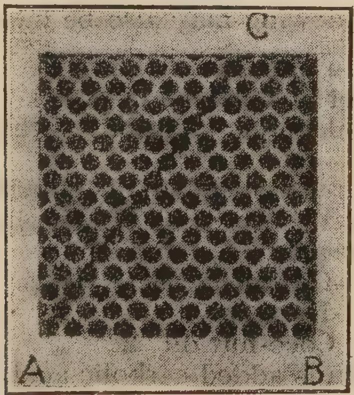
Pyrocide 20—1 part.
Kerosene (2nd quality) 19 parts.

Kerosene (2nd quality) 62 parts.
Liquid extract of pyrethrum 1 part.
Carbon tetrachloride—2 parts.
Oil of citronella—4 parts.
Petrol—11 parts.

Pyrethrum in a water base is used for destroying mosquitoes in aeroplanes.

The Protection of the Individual from bites of Mosquitoes.—Reliance is placed primarily upon the mosquito proofing of houses or the use of mosquito nets. The latter should be employed whenever it is possible in the absence of mosquito proofing. On service, suitable types of bivouac or tent nets should be available and the strictest orders in regard to these should be issued.

Fig. 15.



Shows the correct method of counting the mesh of cotton netting. The mesh of this net is the sum of the counts made along the lines AB and AC, the hole at A being counted twice.

Care is necessary that wire gauze or cotton netting is of the correct mesh to exclude mosquitoes. In the case of the former the mesh is calculated by counting the number of holes to the linear inch. The size of the openings varies with the count to the

inch and also with the thickness of wire used, the latter being expressed in terms of Imperial Standard Wire Gauge. To exclude mosquitoes from buildings, 14 mesh screencloth of 30 I.S.W.G. will suffice in most districts, but when certain small species prevail a 16 mesh of 28 I.S.W.G. is necessary. In the former case the wire is 0·0124 inch in diameter and the apertures measure 0·059 inch.

In the case of cotton netting the mesh consists of two series of holes, the lines intersecting each other at an angle of about 60°. The mesh is the sum of the number of holes counted along both lines within an area of one square inch, the hole at the angle of the square where the two lines meet being counted twice. (Fig. 15.)

The mesh of the nets issued to the army is 28/29 holes to the square inch.

Cotton thread is standardized by weight, being described as "30", "40", "50", etc., the higher numbers indicating the thinner thread. The thread used for army nets is 30/40 cotton (*i.e.* 30 warp, 40 bobbin).

When away from the protection afforded by mosquito nets repellants may be employed. Dover's cream is extensively used for this purpose and has the following composition :—

Oil of citronella	½ ounce.
Spirit of camphor	¼ ,,
Cedar wood oil	¼ ,,
White petroleum jelly	2 ounces.

For army purposes this is issued in 2-ounce containers with screw tops, and camphor and hard paraffin are substituted for the spirit of camphor and white petroleum jelly. It is applied fairly lavishly to exposed parts and is not rubbed in. The effects wear off at a rate depending on temperature, humidity, and perspiration, and with exposures of more than 1½–2 hours further applications will be required.

As repellants, the following may also be mentioned :

(1) Citronella oil in vaseline.
(2) Oil of bergamot in kerosene (1 in 16).
(3) 50 per cent. alcoholic solution of thymol or oil of cloves in lanoline.
(4) Cassia oil as recommended by Howlett. This consists of cassia, 1 part ; brown oil of camphor, 2 parts ; vaseline, lanoline, or salad oil, 4–5 parts.
(5) Bamber oil :—Citronella oil 1½ parts.
Kerosene 1 ,,
Coco-nut oil 2 ,,
To which is added carbolic acid 1 per cent.

NOTE.—The insects most likely to be mistaken for mosquitoes are the harmless midges belonging to the Chironomidæ. These, however, nearly always have the long, narrow abdomen turned up at the end. They do not possess a biting proboscis, and the wing venation differs widely.

Biting Chironomidæ are sometimes confused with mosquitoes, but a glance at their wings dispels the illusion. The intermediate hosts of *Acanthocheilonema perstans* have been shown to be *Culicoides*

austeni and *C. grahami*, the larval development taking seven or eight days. Darkness is essential for infection, and a lamp of ¼ candle power inside a tent seven feet long suffices to repel these culicoids.

SIMULIIDÆ

In some parts of the world these are known as Sandflies.

Diseases transmitted by.—The filarial worm, *Onchocerca volvulus* is transmitted by *Simulium damnosum* in which the larvæ take eight to ten days to reach the infective stage. A closely allied helminth, *O. cæcutiens*, is believed to be transmitted by *S. avidum S. mooseri, S. ochraceum.*

The bites of *Simulium* are particularly severe and painful when they attack in large numbers. The flies are met with during the spring and summer in Europe, and they also occur in many parts of the tropics.

Fig. 16.—*Simulium.*

a. Imago. *b.* Larva. *c.* Pupa.

The Simuliidæ, often called buffalo gnats, are small, dark, hump-backed flies, ranging in size from about a large pin's head to about 6 mm. in length (Fig. 16).

The female *Simulium*, which has a short but formidable proboscis, lays her eggs in gelatinous masses on water-weeds and stones in running streams; these hatch, and small, peculiar larvæ emerge which have a sucker at the posterior end of the body by which they attach themselves to stones or weeds in the stream (Fig. 16, *b*). The pupæ are enclosed in a kind of cocoon. The cocoons and enclosed pupæ are also attached to stones or submerged water-weeds (Fig. 16, *c*).

Preventive Measures.—The elimination of *Simulium* from a district is too great a problem for consideration in a war area. To keep off the adult flies—only the females of which, as a rule, bite—some repellant may be used, such as a lotion of an essential oil made up with quinine or an infusion of quassia. Citronella oil and oil of bergamot have also been recommended. (For other insect repellants *see* section dealing with Mosquitoes.)

MIDGES

One genus only need be considered, viz., *Phlebotomus*, species of which are known in Southern Europe sometimes as "Sandflies" or "Pappataci Flies."

Diseases transmitted by.—Phlebotomus fever (Sandfly fever), oriental sore, and probably kala-azar.

PHLEBOTOMUS

Small flies having the wings and body very thickly covered with hairs (Fig. 17, *a*). In most species only the female sucks blood, and though the flies are minute their bites cause severe irritation. On the slightest disturbance the insect by short rapid flights suddenly moves to left or right, suggesting to some extent the movements of a flea. Its small size enables it to creep through the mesh of ordinary mosquito nets.

Fig. 17.—*Phlebotomus papatasii.*

a. Imago. *b.* Larva.

The fly breeds in such places as dark and damp cellars, caves, dug-outs, cracks and fissures in soil, under damp stone walls, etc. Moist organic matter is essential as well as shelter and darkness. Too much moisture drowns the larvæ and it may be accepted that material for a possible breeding place is too damp if it adheres to the fingers and does not just fall off when rubbed gently between them. The egg hatches and gives rise to a minute caterpillar-like larva, whose body shows, according to the stage of development, either one or two pairs of long bristles at the posterior end (Fig. 17, *b*).

The larva lives on organic matter, and when fully grown pupates, the perfect insect emerging some days later. The cycle of development usually takes one or two months according to conditions.

In order to detect breeding places, large quantities of suspected material should be examined for larvæ. This may be done by filtering through sieves with mesh of decreasing size, down to 40 strands to the linear inch, and finally through muslin, from which the larvæ can be floated in a saturated solution of sugar in water.

Preventive Measures.—The range of flight of the sandfly is comparatively small and the eradication of breeding places within 250 yards of barracks, etc., will do much to reduce the numbers of these insects. It is, however, essential before work of this nature is commenced that a survey should be carried out with a view to preventive efforts being limited to the elimination of cracks, crevices, etc., in which there is a combination of the three essentials, viz.—darkness, moisture, and organic matter.

The following points should receive special attention ;—

(1) Removal of all rubbish, especially heaps of rubble.

(2) Levelling the ground by rolling and, in special cases, by rendering the surface impermeable with cement, asphalt, tar, or similar material.

(3) Facing and pointing of walls of buildings in which crevices have appeared which are likely to afford breeding places for the insects.

(4) The eradication of cracks and crevices in the banks of streams, drains, etc., by smoothing off the surface or lining with cement or concrete.

Adult sandflies in houses and barracks are most easily destroyed by oil sprays (*see* p. 35) or even ordinary light kerosene. Such methods as swatting and flaming with a painter's blowlamp, especially in the early morning when the flies are resting on the walls, may also be employed. Hurricane lamps smeared with vaseline or tanglefoot used at night will trap large numbers of sandflies.

Steps should be taken to ensure that places suitable for harbouring the insect are reduced to a minimum and to this end rooms should be kept clean and clear of cobwebs.

As much natural lighting as possible should be provided and ventilation and air movement should be satisfactory. Each year the interior of all rooms should be washed down, painted, and limewashed.

As regards the protection of the individual, the use of nets is usually not practicable as the mesh necessary (45 to the square inch) reduces air movement to such an extent as to cause grave discomfort or even danger in hot weather. Air currents have a marked deterrent effect and satisfactory fans and punkahs will be effective in keeping the insects away. It should be remembered that sandflies do not fly high and that their numbers are much decreased in upper storey rooms.

Under active service conditions many of the preventive measures mentioned are likely to be impracticable, although in the case of rooms, dugouts, tents, etc., one or other of the sprays mentioned

may prove valuable. Repellants are of importance under such conditions and Dover's cream will give good results. Its composition is given in the section dealing with protection from mosquitoes. Vermijelli is said to be effective, as also oil of cassia or oil of eucalyptus, while the following ointment is a useful one :—

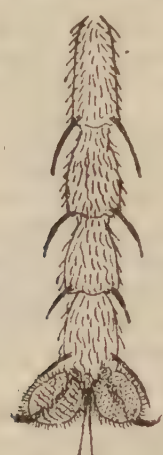
Aniseed oil, Eucalyptus oil, Turpentine oil	of each 3 minims.
Lanoline	1 oz.

HOUSE FLIES

Diseases transmitted by.—The common house fly (*Musca domestica*) is definitely known to contaminate food by conveying pathogenic organisms on its body, wings and legs (Fig. 18), or depositing them in its regurgitations or its droppings. The last-mentioned is the method which has now been proved to occur in amœbic dysentery. The lesser house fly (*Fannia canicularis*) and the latrine fly (*F. scalaris*) have the same filthy and dangerous habits as *Musca domestica*.

Generally speaking, the plague of flies is worst in hot, dry and sandy countries. Bush country, with all its drawbacks, does not

Fig. 18.—*Musca domestica.*



Foot, showing hairs on which bacteria, etc., lodge.

seem to be such a happy hunting ground for the filth-carrying fly as desert lands where sand is plentiful. The climate is also possibly inimical and the abundance of ants which prey on fly eggs and larvæ may have something to do with the paucity of flies.

An important factor in fly breeding is the number of draught animals with a force.

It should be mentioned that *M. domestica* is absent from the greater part of India, where it is replaced mainly by *M. vicina*. This species resembles *M. domestica* closely, the most obvious difference is that the male has not the relatively wide space between

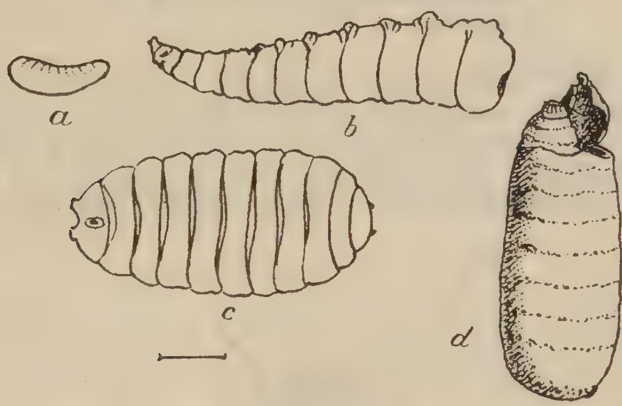
the eyes which is found in *M. domestica.* Two other species of *Musca* habitually come into contact with man in India, *M. humilis* and *M. sorbens* (=*nebulo*). The former has only two longitudinal stripes on the thorax, and in the latter species the eyes of the male are still more closely set than in *M. vicina.*

It is impossible to deal fully with the huge question of flies. Only the more important points receive attention.

Musca domestica

Finds a favourite breeding place in human excrement, in manure, scraps of food and offal and filth generally, provided it is fairly moist. The female lays a large number of eggs, each of which is white, sticky, shiny, cigar-shaped and can be seen by the unaided eye (Fig. 19, *a*). They are usually deposited in batches on the surface of the breeding place, and hatch in from one to four days, according to the temperature. The larva is a small footless maggot, cream-coloured and tapering anteriorly to a fairly sharp point (Fig. 19, *b*).

Fig. 19.—*Musca domestica.*



a. Egg. *b.* Larva. *c.* Pupa. *d.* Empty puparium.

The larvæ feed on the decomposing material in which they have hatched, and when the weather is hot, become fully grown in about five days. They then migrate from the food, and, if possible, work their way down into the subjacent and surrounding earth, where the body shrinks to an elongated barrel shape. They may be found at a depth varying from a few inches to several feet, according to the nature of the soil. The outer skin hardens slowly and later takes on a deep brown colour forming the pupa case or puparium (Fig. 19, *c* and *d*). The pupal stage lasts from three to five days under favourable conditions, and the fly then emerges, working its way through the soil to the surface. In loose sand flies have actually been known to reach the surface from a depth of ten feet. At first the wings are crumpled and folded, and until these expand the flies are often to be seen running over the breeding ground, looking at a

short distance very much like small spiders (Fig. 20). About an hour after emergence the wings are fully expanded, and a little later the fly is capable of flight (Fig. 21). It has been found that under very favourable conditions the whole of the developmental life cycle may be accomplished in so short a space of time as five days.

Fig. 20.—*Musca domestica.*

Just emerged from the pupal case. Note the wings, as yet unexpanded, folded and crumpled on the back of the insect.

There are some other points about flies well worth consideration, for flies mean filth, and, what is more, local filth. A single female fly usually lays about 120 eggs in one batch, and during the year, four such batches. Theoretically this mother fly in six months could become the ancestress of 5,598,720,000,000 adult flies, if all

Fig. 21.—*Musca domestica.*

The common house fly.

her offspring reached maturity and bred, which fortunately is not the case.

Preventive Measures.—Abolish breeding places as far as possible, but unfortunately these are often beyond military control. None the less much may be accomplished by unremitting warfare, and in similar surroundings the best disciplined units will be freest

from flies. It has been estimated that one horse produces sufficient manure to give rise to 40,000–50,000 adult flies a month, which shows the paramount importance in fly prevention of the proper disposal of stable manure. By tight packing the heat and gases of fermentation can be used to destroy fly larvæ. In direct contact with these gases larvæ are killed in one minute at 51° C. and in four or five seconds at 60° C. The heap, as it is formed, may be plastered with puddled earth to form a layer 4 inches to 6 inches thick, beaten down and allowed to dry. If this method of covering the packed manure is not employed care should be taken that the outer surface of the heap is stripped off to a depth of 6 inches after not more than four days and buried in the fresh manure. Another method is to stack manure on an impervious platform, and trap the escaping larvæ at the edges by simple mechanical devices. In hot climates manure may be burned. Protect all larders, food and latrines by screens, nets, etc. Foodstuffs in jugs and basins should be guarded by mosquito-net covers, such as can readily be made from mosquito-netting by cutting out pieces of the requisite size and attaching small weights or beads along the edges. These can be thrown over the mouths of vessels containing food.

A special note is necessary in regard to cookhouses, which are only too often black with flies. If screened they often become mere fly traps, unless the screening is very effectively carried out. If the latter is not practicable it is far better to keep them dark, to have their doors facing North (in the Southern hemisphere, South) to arrange for a good draught through them when it can be managed and to protect the food itself by wire covers and screened cupboards.

Flies are to some extent kept out of cattle sheds by whitewashing the walls with milk of lime to which alum is added in the proportion of 2¼ lb. for each 3 gallons of lime ; this mixture may also be tried in cookhouses.

Destruction of Flies.—Trapping by means of " tanglefoot " and other sticky fly-papers or by means of specially constructed traps. Tanglefoot is a mixture of 5 parts by weight of crude castor oil with 8 parts of crude resin. The mixture is made in double tins with water in the outer tin. The castor oil is first heated to simmer, powdered resin being then added and stirred in. The mixture is allowed to simmer—not boil—for 15 minutes. It is spread on glazed paper or wires. Fly papers act best when they are arched and not laid flat. The wires are hung up. There are many forms of trap which are easily made. Of these the box trap and balloon trap are probably as efficient as any. Fig. 22 shows a simple type of the former.

The following points must receive attention if these traps are to be a success :—

(*a*) The calico or canvas forming the greater part of the sides of the trap should be stretched tightly on the framework.

(*b*) The slit between the wire mesh and the alighting board should be just large enough to allow a bluebottle fly to enter the trap.

(*c*) The trap should, as a rule, be placed in the sun out in the open.

(*d*) It should be placed outside a mess or cookhouse or near a latrine or between an occupied tent or camp and any source of flies.

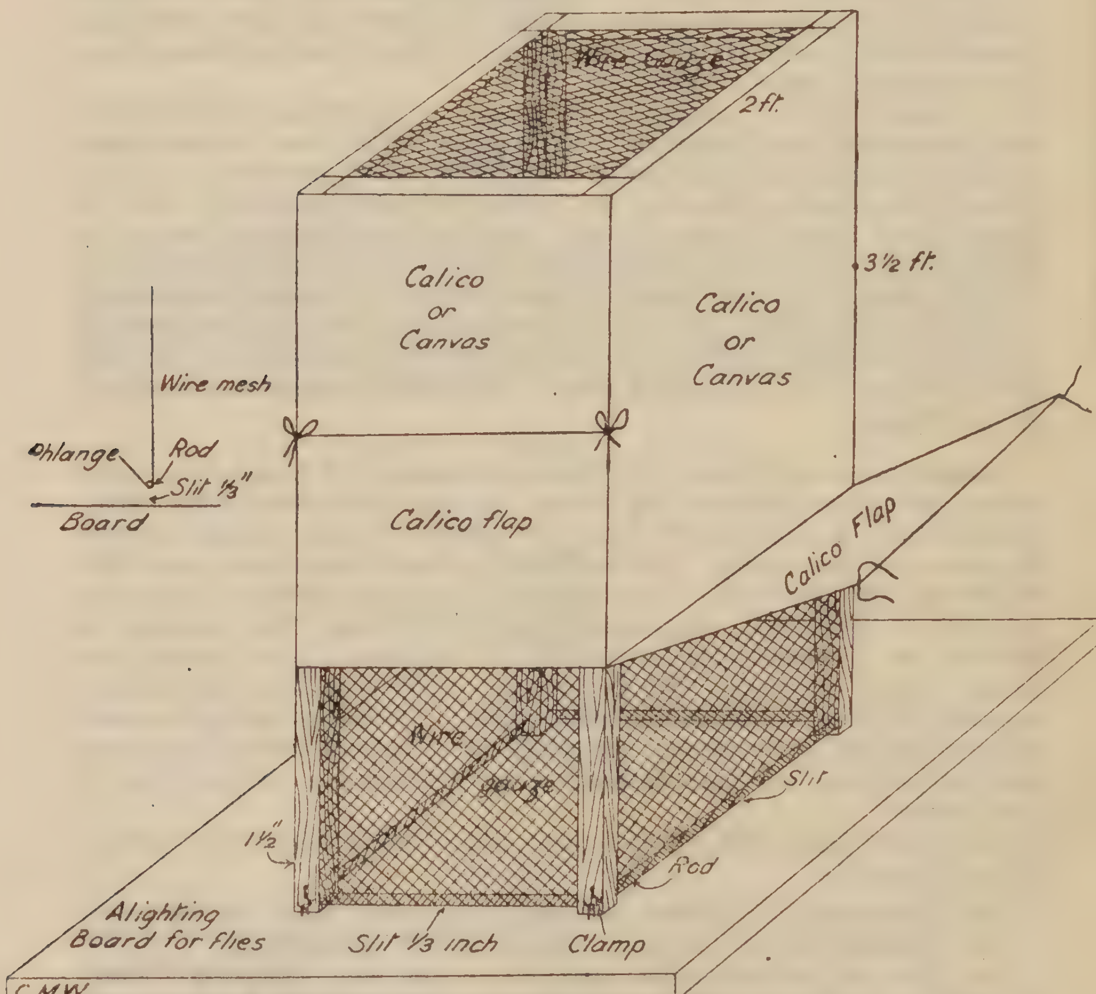
(*e*) It is essential that it should be properly looked after, especially as regards baiting.

(*f*) Any attractive bait may be employed, but one of the very best is chicken entrails. Other baits are raw meat, cheese paste, stale beer, sugar, jam or treacle mixed with beer, fish and fruit refuse.

(*g*) Flies in the trap are best killed by a poisonous solution such as formalin or sodium arsenite, referred to later, and used in a covered tin through the lid of which wicks protrude. These wicks dip down into the fluid which they suck up, and the flies imbibing the poison from them die speedily.

(*h*) Failing poison the flies can be killed by spraying with one of the spray solutions described below, or possibly by fumigation.

Fig. 22.—Cage Fly Trap.



For use outside cook-houses, butchers' shops, mess-huts, or latrines. They can also be placed between a camp and any outside sources of flies, such as a native village The alighting board should be smooth planed wood, and the bait should be placed not directly upon it, but upon trays, pieces of cardboard, tin, etc.

(*i*) A record should be kept of the daily catch. This may be done by weighing the flies or seeing how many will go into a receptacle of known capacity.

Poison Baits.—Formalin and sodium arsenite are the two poisons most commonly used, the solutions being made up as follows :—

1. *Formalin*—

   Formalin, 1 dessert-spoonful.
   Sugar, 1 ,, ,,
   Water, 1 pint.
   *Washing soda, ½ teaspoon.

2. *Sodium arsenite*—

   (*a*) Small quantities :—

   Sodium arsenite, 1 tablet, (15 grains, with sugar and an aniline dye).
   Water, 3½ ounces.
   (or 6 tablets to 1 pint).

   (*b*) Large quantities :—

   Sodium arsenite, 1 lb.
   Sugar, 10 lb.
   Water, 10 gallons.

Formalin is used in dining-rooms and kitchens in simple traps made from glass jars or the like with wicks of blotting paper, lint, or similar materials. It is most effective in the early morning, but care must be taken that no other foodstuffs or water are accessible to the flies.

Sodium arsenite is used chiefly in the roller towel fly traps, which consist of an endless piece of sacking kept moist by being drawn through a metal trough containing the arsenite solution. Traps of this nature should be placed out of doors near latrines and manure heaps, in the shade in sunny weather, and in the open in cloudy weather. Strips of canvas, frameworks of knotted string or small branches of some tree or shrub, the leaves of which will remain on when they dry, may also be dipped in the solution and hung up in safe and convenient places.

The solution may, in addition, be sprayed over refuse and fly breeding places where there is no chance of animals being poisoned. It can also be placed in shallow pans in latrine buildings.

A solution of sodium fluoride 2–5 per cent., along with sugar solution, has proved very efficient as an indoor poison.

These poison baits are often effective in dry climates but may utterly fail to attract flies if the atmosphere is humid.

Spraying with poison.—This is useful indoors for domestic purposes, but is of little value in the field.

1 per cent. oil of wintergreen in 99 per cent. light kerosene causes the instant death of flies when used as a spray.

---

* If lime water is used instead of plain water, this may be omitted.

Lefroy's solution when sprayed on flies paralyses them, but does not kill them and they must be swept up and burnt. Its composition is as follows :—

Pyrethrum powder	2 lbs.
Methylated spirit	1 gallon.
Saffrol	1 gallon.
Aniline	1 ounce.

The following gives good results :—

Kerosene (2nd quality)	62 parts.
Liquid extract of pyrethrum	1 part.
Carbon tetrachloride	2 parts.
Oil of citronella	4 parts.
Petrol	11 parts.

A simple spray which is very effective consists of :—

Soap	$\frac{1}{4}$ lb.
Water	$\frac{1}{2}$ gallon.
Kerosene oil	1 gallon.

Flaming.—This is of definite value. A lighted torch of some sort is passed under flies which have settled on roof, ceiling, rafters, etc., at night. Large numbers may be destroyed in this way.

Swatting.—Wire mesh or leather flaps attached securely to rigid handles are very effective when used as swats. They should be available in kitchens, etc., when flies are troublesome.

THE LESSER HOUSE FLY (*Fannia canicularis*). (Fig. 23.)

This fly belongs to the Anthomyidæ, and in common with other members of this family the distal portion of the fourth longitudinal

Fig. 23.—*Fannia canicularis.*

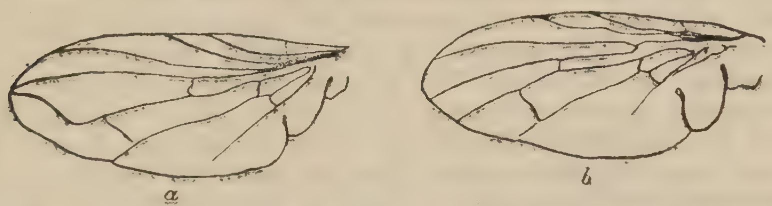
Fig. 24.—*Fannia canicularis.* Larva.

vein of the wing does not bend forwards towards the third vein (Fig. 25). It must be emphasized, however, that neither *M. domestica* nor *F. canicularis* can be identified by their wings alone, for many other flies have exactly the same arrangement of the veins. A useful diagnostic character shown by *F. canicularis* males is a yellowish, translucent patch on either side of the base of the abdomen. The vast majority of flies found in houses in England during the early summer belong to this species.

It usually breeds in old vegetables or vegetable refuse, but a favourite breeding ground is human fæces. The larva is a peculiar dirty-white coloured creature, possessing tassel-like processes from each segment of the body, shown well in the accompanying illustration (Fig. 24). The other stages and details of development resemble those of *Musca domestica.*

Fig. 25.—The wings of *Musca domestica* and *Fannia canicular* contrasted.

NOTE.—These species cannot be identified by their wings alone.



a. Wing of *M. domestica*. Note upturning of the distal portion of 4th longitudinal vein towards the 3rd vein.
b. Wing of *F. canicularis*. 4th longitudinal vein not upturned.

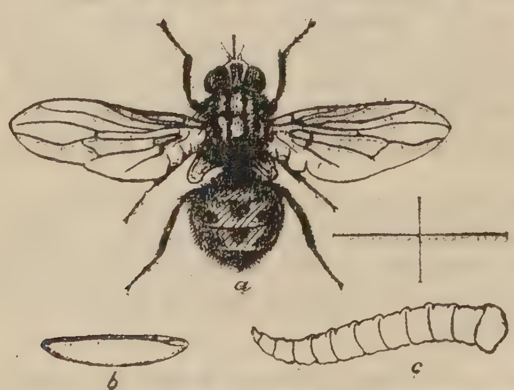
Since the larvæ of the fly often live in vegetables they sometimes find their way alive into the human intestine, thus causing a form of intestinal myiasis.

Preventive and Destructive Measures.—As for *Musca domestica*, except that the favourite breeding place of this fly must receive special attention.

THE STABLE FLY (*Stomoxys calcitrans*). (Fig. 26.)

As will be seen, this fly is rather like the house fly, but it has a spotted abdomen and is a blood sucker, being furnished with a stout

Fig. 26.—*Stomoxys calcitrans.*



a. Imago. *b*. Egg. *c*. Larva.

proboscis. The inclination of the distal portion of the 4th longitudinal wing vein is intermediate between that of *Musca* and *Fannia*. (Fig. 26, *a*.)

It commonly attacks animals, biting mules and horses about the fetlocks, and drawing scarlet beads at every thrust. It has been

said to carry the virus of poliomyelitis. *Stomoxys* probably acts as the mechanical vector of many important diseases, notably surra, an important veterinary disease due to *Trypanosoma evansi*.

Many species of *Stomoxys* occur throughout the world. *S calcitrans* is the only one found in Europe.

TSETSE FLIES

The tsetse flies, *Glossina*, constitute a genus of the family Muscidæ, and are found only in Africa and Arabia. They are brownish flies and are distinguished by certain peculiarities in the wing venation. The course of the fourth longitudinal vein is characteristic of *Glossina*. It curves strongly forward to join the obliquely placed anterior cross-vein, and, bending forward again at its junction with the posterior cross-vein, it touches the margin of the wing at a point much anterior to the tip. The cell lying between the proximal portion of the fourth and fifth veins has some resemblance to a butcher's cleaver. A comparison of Fig. 21 and Plate 3 will illustrate this characteristic appearance. The fly deposits at a birth a single mature larva (Plate 5) in a carefully selected spot. A favourite site is under trunks of fallen trees, and a light soil with some degree of shade is essential. Immediately after birth the larva buries itself and pupates. The duration of this stage varies, but it is often from three to four weeks, the time depending largely on the temperature. The pupa case is ovoid and easily recognizable by the two posterior protuberances (Plate 6).

There are about twenty species of *Glossina*, and of these *G. palpalis*, *G. morsitans*, *G. tachinoides*, *G. brevipalpis* and *G. swynnertoni* have either been infected with " human " trypanosomes, or otherwise implicated in the spread of sleeping sickness. *G. palpalis* (Plate 4) and *G. morsitans* (Plate 3) are the most notorious species. The banks of lakes and rivers overhung by trees and scrub form the favourite abode of *G. palpalis*. Its natural range from water rarely exceeds thirty yards, though it may follow victims considerably farther. *G. morsitans* is much less restricted in its haunts than *G. palpalis* and inhabits as a rule moderately wooded country, and is not dependent on the propinquity of water. It does not occur continuously throughout suitable country, but tends to be restricted to limited belts.

As is well known, tsetse flies are attracted by rapidly moving objects like motor-bicycles and motor-cars. They have a quick darting flight, so that the tsetse seems to " come out of nowhere," so suddenly and, as a rule, silently does it arrive, and so lightly does it settle on its victim.

Prophylaxis.—Breeding places may be dealt with by the clearance of jungle, scrub, etc., for a distance of thirty yards from the banks of lakes, rivers, or streams.

Fly spots where there are landing places, ferries, wells, or roads, should receive special attention in this way if they cannot be avoided altogether.

Trapping of the flies may be effected by various means ; coolies in white with dark cloths on their backs smeared with bird lime have

been employed for the purpose and are sent out into the jungle each night. Many hundreds of flies may be caught in this way.

Harris's trap is of value. It consists of a framework of light wood covered by Hessian cloth and is roughly triangular in section with a flat uncovered top. The latter is 6 feet long by 3 feet wide, the sides converging below to about 3 inches apart with a narrow open slit along the bottom. The trap is hung so that the open slit is 48 inches from the ground. A wire gauze cage is fixed to the upper surface and the wire gauze so arranged that the flies cannot return to the hollow body of the trap. Such traps are best hung on the sunny aspects of the flies' haunts.

Tsetse flies have a tendency to settle on moving objects such as the backs of pedestrians or cyclists, or on the hoods of motor cars, and may be carried for miles in this way. On this account restriction of vehicles to fixed routes may be necessary and the subjection of motorists and cyclists to prescribed measures. White troops operating in tsetse fly belts, especially motor transport drivers and dispatch riders, should be provided with veils and gauntlets, and, if the region is known to be a sleeping sickness area all troops should be provided, as far as possible, with suitable nets. Horses should be similarly protected.

THE CONGO FLOOR-MAGGOT FLY

This fly, *Auchmeromyia luteola*, is chiefly of importance in that it is the parent of the well-known Congo floor-maggot, the only dipterous larva known to suck human blood. Although first discovered in the Belgian Congo, the maggot is not well named for it is widely distributed in tropical and sub-tropical Africa.

It was frequently found in the East African war area and is of some interest, as, owing to its peculiar habits, its presence causes natives to vacate huts which harbour it.

The Fly.—It is rather a stoutly-built fly, orange-buff in general colour, but with the distal end of the abdomen blackish. Plate 7 shows the fly, which is rather like the Tumbu fly, ***Cordylobia anthropophaga*** (Plate 8), but differs from it because in *A. luteola* the eyes are wide apart in both sexes and the second abdominal segment in the female is twice the length of the same segment in the male, which is not the case in *Cordylobia*. *A. luteola* has also a narrower and more elongated body than *C. anthropophaga*.

A. luteola, which is a non-biting fly, feeds on blood, on fallen fruit and dejecta and seems to be sensitive to heat. The female is oviparous, laying about 80 eggs at a time. The eggs are deposited in damp soil, possibly in places where the ground has been fouled by urine or excrement and therefore either in native huts which the female fly haunts or in their neighbourhood.

The Larva.—It hatches from the egg, avoids the light and buries itself in dust or earth. Its life, prior to pupation, varies from fifteen to seventy-six days, the duration depending on conditions of food and temperature. It is very resistant to starvation, but when starved is very sensitive to heat, a property not exhibited when it is well fed. It may be this thermotropism which guides it to its host in search of food.

The maggots are most numerous in the floors of huts in which people sleep on the ground. Plate 7 shows the larva, which is of a dirty white colour save when gorged, and has eleven segments, the apex of the anterior segment being furnished with two black hooks. Between them is the oral orifice. These blood-sucking larvæ feed at night, but do not attack people sleeping on high beds. When full of blood they acquire a bright red colour and in this condition can often be dug out of crevices in the earthen floors of huts.

They are not known to convey any disease, but, if numerous, may extract comparatively large quantities of blood from their sleeping victim.

Prophylaxis.—General cleanliness and the enforcement of sanitary measures. The use of high beds. Sleeping mats and blankets should be searched for eggs and larvæ as it is possible the latter may be transported in such impedimenta. Infected huts can be rendered habitable by firing the ground or by digging up floors and removing the surface soil, which can then be disinfected.

CARCASE FLIES

Under this term several genera are considered, including the "Bluebottles" (*Cynomyia*, *Calliphora*, etc.), the "Green-bottles" (*Chrysomyia*, *Lucilia*, etc.) and *Sarcophaga*—the hairy, grey-coloured flies found on decomposing material.

Diseases transmitted by.—It is more than probable that the "Bluebottles" and "Greenbottles" convey bacteria and protozoa to foodstuffs. Such flies were responsible for the cases of external myiasis (wound infection) commonly met with in France and elsewhere during the last war. But such infestations were not without compensation, for the larvæ removed dead and damaged tissues, and so tended to prevent the development of gas gangrene.

"Bluebottles"

This term includes the common *Calliphora*, large flies with a dull thorax and an abdomen of a deep blue metallic lustre. They are the largest of the brightly burnished flies, and, in addition, the cheeks are very hairy.

"Greenbottles"

This term includes several genera, and is applied to flies whose bodies show a very bright lustre, ranging in shade from a vivid blue-green to a green-bronze, and they are not so hairy as the former flies.

Chrysomyia and *Lucilia* are the most important genera and species of both are a frequent cause of myiasis. *Chrysomyia* usually shows darkish cross bands on the abdomen, but the best differential character is the poorly-developed bristles on the dorsum of the thorax, whereas in *Lucilia* these are large and stout.

Sarcophaga

These are grey, very hairy flies with three dark longitudinal lines on the thorax. The different species vary greatly in size, from about that of *Musca domestica* to something considerably bigger than a bluebottle.

The life-history of these insects corresponds in most details, except that in some species of *Sarcophaga* the female gives birth to living larvæ and does not lay eggs.

Female "Bluebottles," "Greenbottles" and some *Sarcophaga* deposit numerous white, cigar-shaped eggs on decomposing material, which is a carcase for choice, and these hatch very rapidly to small, active, cream-coloured larvæ or maggots (Fig. 27, *b*). The maggots feed voraciously, and by means of two powerful claws that are situated within the mouth, and can be protruded, are able to tear and consume all animal tissues, including soft bone, at a truly remarkable rate.

Fig. 27.—*Sarcophaga sp.*

a. Imago. *b*. Larva.

With a plentiful food supply and warm weather, the larvæ attain full growth in a few days, then migrate, if possible burrowing into the earth, where they pupate, emerging as flies some days later.

So long as they confine their attentions merely to carcases and other decomposing material these insects may be considered harmless and excellent scavengers ; but they may lay their eggs or larvæ on exposed wounds, or in the natural orifices of the body. The larvæ attack the living tissues, burrowing oftentimes deeply and causing great damage, which sometimes leads to fatal results.

Some species of *Chrysomyia*, *Sarcophaga*, etc., are obligate producers of myiasis, for they are unable to live in carcases and require living tissues for development. For treatment, *see* Myiasis

HIPPOBOSCA

On horses and other animals in the East, there will often be noticed dark, flat, leathery, yellow-marked, ugly-looking flies, which at a distance resemble ticks (Fig. 28).

These are the Hippobosca, which suck the blood of cattle and horses, but do not attack man. They will often be found clustering under a horse's tail, and cause the animal much discomfort. When disturbed they shift about on the skin in a sidelong, crawling manner like that of a crab. Occasionally they will settle on a man or his clothes, where they cling closer than a brother and give rise to a

sensation of loathing. They are easily caught by the hand and are best killed by pulling off their heads, their hard leathery bodies being very resistant to pressure.

Melophagus ovinus, an entirely wingless hippoboscid fly, known as the sheep "tick" or "ked," transmits the non-pathogenic trypanosome of sheep, *Trypanosoma melophagium*.

Fig. 28.—*Hippobosca.*

Note.—Mention should be made of the large yellow and brown hornets which infest Basra in Mesopotamia. They feed greedily on fæces and as, after feeding, they frequently visit water, they may pollute water supplies, possibly after these have undergone sterilization. Hence they are undoubtedly a source of danger. They are easily trapped by the methods employed for wasps in this country.

BERIBERI

The classical result of vitamin B_1 deficiency is beriberi, a disease characterised by multiple neuritis, muscular atrophy, cardiovascular changes, and often a massive œdema. Beriberi is endemic in those areas of the Far East where the chief article of diet is rice. It is well known in parts of Africa and South America. In Europe and North America, apart from small outbreaks in prisons and institutions, it does not occur in epidemic form except under conditions of war and famine ; but sporadic cases are seen in individuals who fail to ingest or absorb sufficient amounts of vitamin B_1, through causes such as alcoholism, gastro-intestinal disease, mental disease, dietetic faddism, or poverty.

Etiology.—Vitamin B_1 (also known as aneurin or thiamine) plays an important part in the processes of oxidation in the body : combined with phosphoric acid it forms a co-enzyme (co-carboxylase) for the oxidative breakdown of carbohydrate. In vitamin B_1 deficiency carbohydrate oxidation cannot proceed beyond pyruvic acid, and this intermediary metabolic product accumulates in the tissues and can be demonstrated in increased amounts in the blood. Beriberi

does not develop in starvation, when the energy needs of the body are derived chiefly from the reserves of body fat.

Pathology.—In beriberi with massive œdema ("wet" form), the right auricle is often huge, with a very thin wall, while the right ventricle, though dilated, has a thickened wall; the conus arteriosus is tremendously dilated. Microscopically, there may be no abnormality or some hydropic degeneration of the muscle fibres and separation of the muscle bundles due to œdema. The organs, especially the liver, show evidence of chronic venous congestion, and the subcutaneous œdema is accompanied by anascara and œdema of organs and tissues. It is still uncertain whether the œdema is a simple transudate due to congestive cardiac failure or whether it is the result of some specific effect of the vitamin deficiency such as increased capillary permeability or even serous inflammation.

Nerve lesions are found in the chronic type of beriberi ("dry" or neuritic form) and in mixed cases where wet beriberi is accompanied by neuritic symptoms. The lower extremities are most commonly affected, but the cranial and cervical nerves, particularly the vagus and phrenic, and those of the trunk, may also be implicated. Microscopically there is a pan-neuritis, beginning with degeneration of the myelin sheath and progressing to fragmentation of the axis cylinders and Wallerian degeneration. The central nervous system shows relatively few changes.

Symptoms.—The body has only a limited storage capacity for vitamin B_1, and experimentally symptoms of deficiency may appear in ten days if the vitamin intake is reduced to a very low level. Under natural conditions, however, the fully developed disease appears only after about three months. One of the earliest symptoms is a feeling of epigastric fullness and discomfort, often accompanied by tenderness over the duodenum; for this reason the Chinese coolies in Malaya call beriberi by a name signifying "indigestion." Subjects of the disease often ignore these early symptoms and report sick later, complaining of weakness of the legs and numbness of the feet. Usually the anæsthesia commences on the inner side of the ankles and wrists, spreading up and down, the sense of touch being blunted rather than lost. Anæsthesia may be limited to the limbs, but parts of the trunk may be affected also. The face is very rarely involved. The fumbling fingers of beriberi may be detected on asking the patient to button his coat. Abnormal sensations, such as formication, tingling and a feeling of numbness may appear, and the calf muscles may be tender on pressure, a very usual and characteristic sign. Tenderness may also frequently be elicited by pressure on the popliteal nerve in the popliteal space.

Paresis affects the legs in particular, but the arms are often involved as well; the muscles of the trunk and face usually escape. In the legs the weakness may be apparent first in the extensor muscles of the ankle, spreading to the calves, extensors of the knee, and the thighs; while in the arms the extensor muscles of the wrist, of the fingers, and the muscles of the forearm and arm may be involved in turn. Sometimes in severe cases the respiratory muscles including the diaphragm are attacked. Ankle-drop is common, causing a steppage gait if the patient can still walk, and wrist-drop is met with, but less frequently.

The knee-jerks, at first exaggerated, disappear about the third day as a rule, but occasionally they persist; in one group of fifty cases of marked and undoubted beriberi examined by the writer the knee-jerk was completely absent in forty-eight. The superficial reflexes are generally retained.

Wasting and weakness of the affected muscles is a prominent feature, and their electrical reactions may be altered. The "squatting test" (*see* Diagnosis) is usually positive.

Some degree of œdema is invariable in established beriberi and appears first over the front of the tibia. It may remain confined to this area, but often spreads causing extensive general dropsy, with perhaps effusion into the abdomen, lungs, and pericardium, thus providing a connecting link with another deficiency (or toxic) disease, epidemic dropsy. There may be curiously localized patches of œdema on the body surface varying in size from time to time, and disappearing as suddenly as they came. This so-called wet beriberi may pass into the dry atrophic form, leaving the patient little better than a skeleton.

Involvement of the heart, seemingly due to œdema of the cardiac muscle, is an alarming and often fatal complication. Palpitation and dyspnœa, perhaps on the slightest exertion, cardiac oppression and distress, and cyanosis, may be in evidence as well as all the auscultatory signs of a failing heart. The onset of heart symptoms may be so sudden and acute as to constitute a cardiac crisis.

Generally there is no fever, and constipation is the rule. Vomiting is a bad sign. The urine is diminished with the onset of œdema, and increases in amount as the œdema passes off. Beriberi does not cause albuminuria. In the fully developed disease the blood shows an increase of lymphocytes and a diminution of eosinophiles.

The disease may drag on for weeks and months, with eventual recovery or death from cardiac failure or from some complication.

In the acute fulminating variety, death may take place during a sudden cardiac crisis before the ordinary signs of the disease are manifest.

The mild or latent form of vitamin B_1 deficiency is of even greater importance than frank beriberi, because of its insidious ill-effects on greater numbers of people. The symptoms may be :—

(1) *General*, including weakness and excessive fatiguability, loss of weight, headache, nervousness, loss of power of concentration, and other psychoneurotic symptoms.

(2) *Neurological*—vague neuritic pains, weakness, stiffness, and cramps in the lower limbs, paraesthesiæ, and tenderness of the calf muscles.

(3) *Gastro-intestinal*—anorexia, dyspepsia, flatulence, and constipation.

(4) *Cardio-vascular*—dyspnœa on exertion, palpitation, and perhaps slight œdema of the legs.

Objective signs are few. There may be tenderness of the muscles of the legs on pressure, areas of increased or blunted cutaneous sensibility; increased or later decreased knee and ankle jerks; an otherwise unexplained tachycardia; or slight enlargement of the heart, especially to the right, with systolic murmurs, over-active pulsations, and sometimes a slight increase in the systolic blood pressure.

Symptoms of vitamin B_1 deficiency, and even of classical beriberi, may be precipitated by factors increasing the vitamin requirements (*e.g.* fever or very heavy work) or interfering with its ingestion or absorption (*e.g.* diarrhœa).

Diagnosis.—This rests on an analysis of the diet, the history, physical examination, and the results of a properly controlled therapeutic test. Where symptoms and signs are few and equivocal physical examination should include the "squatting test." The patient, with his hands on the top of his head, is unable to assume a squatting position and to rise from it unaided. If he is squatting and has to rise he accomplishes the act by climbing, as it were, up his own legs. An examination of the heart condition is all-important.

Differential Diagnosis.—As the syndrome presented by beriberi is closely simulated by that presented by other diseases, an attempt must always be made to discover the particular dietetic fault.

It is important to differentiate the early diarrhœa or dysentery of beriberi from dysentery due to other causes.

Amongst other diseases which may cause diagnostic difficulties may be mentioned valvular heart disease, peripheral neuritis, ancylostomiasis, and, in œdematous cases, nephritis. The distinction from tabes dorsalis is important and depends on the absence of lightning pains, Argyll Robertson pupil, etc. Scurvy may closely simulate and may also accompany beriberi as has been recorded in many historical accounts of the combined syndrome. The presence of spongy swollen gums, loose teeth, hard brawny swellings about the ankles and the characteristic hæmorrhages met with in the former should suffice to distinguish the two diseases.

Do not mistake evening puffiness of the ankles, not uncommon during hot exhausting weather, for the œdema of beriberi. Hysteria may simulate beriberi to some extent, but the anæsthesia is usually more extensive, perhaps only the palms and soles escaping, the knee-jerks are not lost, and the paresis is more apparent than real; a seemingly helpless patient may be able to feed himself and button his clothing without difficulty.

Prophylaxis.—None of the common foods are very rich in vitamin B_1, so the daily vitamin requirements must be met from many sources. The vitamin B_1 content of modern diets has been reduced by the milling of cereals and canning of foodstuffs. Rich sources are nuts, legume vegetables including dried peas and beans, fresh meat, especially viscera or pork, and wholemeal cereals. Parboiled rice, although milled, has almost as great an antineuritic potency as undermilled rice, because vitamin B_1 from the pericarp penetrates the endosperm during the boiling process; its keeping qualities are probably as good as those of polished rice, whereas undermilled rice does not keep well.

Yeast is a useful supplementary source of the vitamin. Supplies can always be obtained from Army bakeries mixed with the liquid of the brew; half a pint of this may be taken daily, sweetened with sugar and flavoured with lemon. A dried yeast, rich in vitamin B_1, can also be given in the form of tablets. The yeast extract Marmite has been much used but loses some of its vitamin B_1 content on storage, and should not be relied on as the sole food supplement.

Treatment.—This is chiefly dietetic, and the two most important measures are :—

(1) Give a diet rich in all vitamins and well supplied with high grade protein (since hyoproteinæmia may play a part in the causation of the œdema).

(2) Give adequate doses of vitamin B_1. While concentrates such as yeast, Marmite and Bemax are valuable as prophylactics, by far the best preparation of vitamin B_1 to use in curative treatment is the crystalline vitamin itself. Initial doses should be large, *e.g.* 10–20 mg. (3,000–6,000 International Units) per day, or even up to 40 mg. The vitamin may be given by mouth in tablets of 3 mg., but in very severe cases a solution of the vitamin in the above doses should be injected intramuscularly or intravenously.

After the major symptoms have disappeared, the pure vitamin may be replaced by one of the concentrates mentioned, provided the patient receives about 10 mg. of vitamin B_1 daily. "Tikitiki" is a useful form of vitamin B_1 concentrate ; it can be prepared by sifting rice polishings, obtained fresh from any rice-mill, to get rid of husks and foreign matter, and then extracting the polishings with twice their volume of alcohol.

All patients with severe beriberi must be nursed in bed to minimise the risk of severe cardiac failure. Rest, by reducing energy expenditure, also lessens the requirement for the vitamin.

In acute heart failure, venesection may be a life-saving measure, and oxygen may be administered. Digitalis and other cardiac tonics are less effective than vitamin B_1 in adequate doses.

During convalescence, a close watch must be kept on the heart, and if tachycardia is excessive the patient must go back to bed. Massage and electricity are required to restore the tone and function of the muscles.

BLACKWATER FEVER

Definition.—Known also as malarial hæmoglobinuria or hæmoglobinuric fever, this condition is essentially an acute hæmolysis of uncertain causation, resulting in hæmoglobinæmia and hæmoglobinuria, and associated with inadequately treated malaria. It is entirely distinct in its pathological nature and mechanism from a malarial attack, but malarial infection is an essential factor in its causation.

Distribution.—It is found wherever there are hyper-endemic foci of malaria, and in such places M.T. infection is always predominant—on the west coast of Africa in the deltas of the Congo, Niger and Gambia rivers ; in East Africa along the Zambesi ; in Uganda ; on the upper Nile and in Algeria. In Europe, it is found in Bulgaria, Albania, Greece and Sicily, and, of recent years, it has been in-

creasingly common in Macedonia. In Asia, it is met with in Palestine, especially in the Jordan valley; in India, in Behar, Assam, the Dooars and the Terai, foothill areas of the Himalayas; in Indo-China and in Formosa. In America, it is found in the southern portion of the United States, in the West Indies and in Venezuela. From the Panama Canal zone it has disappeared since the introduction of anti-malarial measures.

The disease is one that attacks *visitors* to the malarial hyper-endemic areas. It is rare in the indigenous inhabitants of tropical regions. These visitors need not be Europeans, *e.g.* labourers moved to build the Corinth canal, Chinese labour to build the Congo railway, Bengal clerks employed in the Punjab, have all shown a high incidence. It is possible that the recent increase in Macedonia is due to the great influx of refugees into that country since 1925. While this visiting factor is definite, there is, however, a necessary residence in the area, usually about one year.

Etiology.—The conditions which conduce to an attack of blackwater fever are :—

(1) The existence of intense endemic malaria.

(2) Reinfection with malaria appears to be an important factor. It is seldom that any first infection, however severe, causes hæmoglobinuria.

(3) Residence in the endemic area has usually been over six months and under five years.

(4) The individual has usually suffered from several attacks of malaria and these have commonly been insufficiently treated. The previous attacks need not have been severe; they may have been minimal or, especially if suppressive quinine has been taken in an irregular fashion, may have been unnoticed.

(5) Heat, cold or fatigue may precipitate an attack. Alcoholism predisposes. Other drugs have been incriminated. Pamaquin, arsphenamine, quinine and even mepacrine have been blamed.

It must be admitted that our knowledge of the cause of this condition is defective. Of its very close association with malaria there can be no doubt and many believe blackwater to be merely a clinical syndrome arising in the course of a malarial infection and dependent on conditions which will be discussed immediately but very briefly. Others regard it as a disease *sui generis*, due either to some hitherto undiscovered blood parasite, or to a specific toxin with hæmolytic properties and only operative in cases where the blood has already undergone change as in malaria and tick fever.

The most generally accepted theory is that blackwater is a manifestation of malarial toxicity in persons saturated with malaria, the attack being determined by various depressing factors or by quinine. The toxin may have hæmolytic properties, and it has been suggested that it is manufactured in the patient's body as a result of auto-immunization against his own red cells. In addition, the red cells are damaged by the malarial parasite.

There are various modifications and amplifications of this view, some laying stress on the presence of acidosis, some stating that the hæmoglobinuria is due to a hæmoglobinæmia, *i.e.* free hæmoglobin in the blood plasma, and not to a hæmolysinæmia, others considering that the administration of sulphates or of acid salts of quinine plays a part, yet others invoking a theory of anaphylaxis. Blacklock suggests that the noxious agent is lactic acid, which he states causes hæmolysis *in vivo* and *in vitro*, and accumulates through deficient oxygenation of the blood due to anæmia.

Hamilton Fairley has shown recently that the pigment present in the blood of cases of blackwater fever is pseudomethæmoglobin (methæmalbumin), previously wrongly described as methæmoglobin. This pigment appears in the plasma and *never* in the red cells or urine; it originates from extra-corpuscular hæmoglobin and, in fatal cases, increases progressively until death. The pigments found in the urine are oxyhæmoglobin, methæmoglobin, urobilin, and hæmatin. The last is supposed to cause the blockage of the renal tubules which may end in anuria, uræmia, and death.

Nothing certain is known except the undoubted fact that hæmoglobin is set free in such quantities that the liver cannot cope with it and convert it into bile pigment. Hence it appears in the urine. In many cases the liver is extensively damaged and in those showing anuria there is a mechanical blocking of the renal tubules by blood debris, *i.e.* hæmoglobin casts.

Symptoms.—The usual course of a case is as follows:—Under the conditions already mentioned the patient feels himself in the grip of what seems to be one of his old malarial chills. He realizes, however, that it is more severe than usual and he feels prostrated by it. He may have been feeling out of sorts for some days and may have noticed that his conjunctivæ have taken on a yellow tinge. On the other hand, the attack may be very sudden, the patient starting to shiver and shake, developing a headache, lumbar pain, and a nausea which soon ends in retching and vomiting of bile. He often suffers from epigastric or hypogastric pain. His temperature mounts rapidly and he finds himself passing a dark urine which may vary in colour from a reddish hue to that of black coffee and has a heavy deposit. His liver and spleen enlarge, his skin is hot and dry and soon develops a jaundiced tint which rapidly deepens. The rapid pulse soon becomes weak, compressible, and of low tension. Sometimes there is constipation, sometimes bilious diarrhœa. The symptoms increase in severity and then, in a favourable case, the skin begins to act freely, the temperature falls and the urine slowly clears, leaving the patient exceedingly weak. The hæmoglobinuria usually lasts about two days. There may be no more pyrexia, or recurrence of fever may take place next day and perhaps for several days. In bad cases the temperature runs a remittent or even a continuous course for several days. High fever, mental confusion, persistent vomiting, hiccup, profuse diarrhœa, and a diminution in the quantity of urine passed are bad signs. Blackwater fever cases usually die from hæmolysis, anuria, or hyperpyrexia with coma. The hyperpyrexia may set in after the urine has entirely cleared.

The great derangement in liver function which occurs should be borne in mind, as the jaundice and some of the cerebral symptoms are probably due to this cause.

Four clinical types of the disease are described.

(1) *Mild to moderate uncomplicated type.*—This accounts for the majority of cases seen. Hæmoglobinuria is definite, the colour of the urine varying from bright red to dark brown, and may last from a few hours to about three days. The intensity of the hæmoglobinuria is usually greatest at first and gradually diminishes. The amount of urine passed is usually normal. If, in treatment, a large amount of fluid is given there may be polyuria, and there is no evidence of retention of non-protein nitrogen in the blood, nor of abnormality of kidney function. With, or soon after, the cessation of the hæmoglobinuria, the temperature falls to normal. Vomiting may or may not occur, and icterus and subsequent anæmia are slight. There is no anuria and toxic manifestations are few. Recovery is the rule.

(2) *Fulminating or toxic type.*—This is characterized by the intensity of the hæmolytic process, the intensity of the accompanying toxic manifestations and the rapidity with which a fatal issue usually ensues. There is no previous indication that a case is to be of this type. The onset is with a severe rigor, and the urine is dark brown from the commencement. A polyuric condition develops, each specimen of urine showing more hæmoglobin than the last. This polyuria appears in spite of the great loss of fluid from vomiting, which is severe, and which prevents replacement of fluid by the mouth. The temperature, high after the initial rigor, tends to drop. Hiccup is marked and delirium common before death, which may occur very soon. In a case which survives more than twenty-four hours, jaundice is intense and the anæmia is profound.

(3) *Anuric type.*—The anuria which may develop in a first or subsequent attack cannot be anticipated. It may appear early or late—usually early. When suppression occurs there is almost total anuria, but usually 50 to 100 c.cm. of urine may be obtained by catheter. The urine thus obtained is bile-stained and, from the high degree of albuminuria, has the appearance of serum rather than of urine. The temperature falls after the initial pyrexia and tends to remain subnormal. Since the whole burden of disposing of the hæmoglobinæmia has fallen upon the liver, the gravest degree of icterus is seen in this type. Life, in these cases, is often surprisingly prolonged up to the eighth or tenth day. In spite of high nitrogenous retention, uræmic symptoms may not appear, and the patient, far from being comatose, may be mentally alert. Vomiting is usually severe, but it may cease a few days before death. Occasionally the liver would seem to have been able to compete with the hæmoglobinæmia and the icterus may clear up.

(4) *Continued or intermittent type.*—In this type the hæmoglobinuria clears up only to recur or it may be continuous. With continued or recurrent hæmolysis the temperature remains high. Oliguria is not seen in these cases. Jaundice is usually well developed. Vomiting and hiccup are rather infrequent and sub-

jective symptoms are few. The anæmia is always intense and is the real danger. This type tends mostly to recover.

There is apt to be a run of comparatively mild cases ending favourably and then a series of severe cases, every one of which may prove fatal. Hence caution must be exercised in attributing success to any special line of treatment.

Morbid Anatomy.—As explaining the symptoms it is well to mention that the chief pathological findings are those of malaria, but that focal necroses of the liver and spleen suggest the presence of a toxin. The bile is inspissated, the kidneys enlarged and congested with deep purple pyramids. The tubular epithelium is degenerated and the tubules choked with granular material and hæmoglobin casts.

The urine shows a copious granular sediment, the nature of which has not been definitely determined. Hæmatoidin crystals may be present and occasionally, but rarely, a few red cells.

Complications.—The passage of blood or hæmoglobin from the bowel may be mentioned.

Diagnosis.—The condition of the urine is the chief guide. It has usually been taught that while malarial parasites may be found in the peripheral blood prior to the attack, they disappear once the hæmoglobinuric condition is fully established, or at least are very difficult to find. There can be little doubt that such a view requires some modification, for if the thick film method be employed, the percentage of success in the discovery of the parasites will undoubtedly materially increase. At the same time, there are cases where the blood is apparently free from plasmodia; and, indeed, an attack of blackwater may actually cure a malarial infection by breaking down the host cells and wholly destroying the intracorpuscular parasites.

When parasites are present, they are usually scanty. Cases of M.T. infection with high fever and large numbers of parasites in the peripheral blood do not, as a rule, develop blackwater fever. Cases are recorded in which only *P. vivax* and, in a few cases, only *P. malariæ* parasites have been found, and these species have been incriminated as causative, but it is generally believed that the disease is due only to *P. falciparum* infection, even although the parasites may be so scanty as not to be found after repeated examination of thick and thin smears.

Differential Diagnosis.—This is not difficult save in paroxysmal hæmoglobinuria, which appears to be uncommon in tropical countries, in a hæmoglobinuric condition induced by quinine alone, and in sickle-celled anæmia. Bilious remittent fever is a severe form of malaria in which there is jaundice and liver failure and in which the urine is dark owing to bile ; but here, as in the case of yellow fever, spirochætosis icterohæmorrhagica and infective hepatitis, the cardinal sign of blackwater, namely hæmoglobinuria, is absent.

Prognosis.—The hæmorrhagic and fulminating toxic types end fatally. Anuria is always serious. Cases with intermittent attacks

of hæmoglobinuria and rigors are also apt to do badly: in these jaundice is slight but anuria frequent. In ordinary cases a great deal depends on the patient's surroundings and how he is nursed. The medical officer should never abandon hope. If he does not spare himself and proceeds on the lines indicated he may have the satisfaction of seeing even a very grave case recover.

Prophylaxis.—With our present knowledge all that can be said is that malaria prophylaxis is also the method to prevent blackwater. Such prophylaxis, so far as quinine is concerned, must be properly carried out. Those who take quinine regularly and in sufficient doses (*see* Malaria) do not contract blackwater fever. On leaving an area in which malaria is hyper-endemic, those who have been accustomed to taking quinine (or mepacrine) should continue to do so for at least two months after arrival in Europe. A majority of the cases of blackwater fever occur in individuals who have failed to take this precaution and later take a large dose of quinine for a suspected relapse of malaria. Chills and excesses of all kinds should be avoided.

Treatment.—In every case, no matter how slight, this spells absolute rest in bed and skilled and careful nursing. If it can possibly be avoided a blackwater patient should never be moved from the place where he is taken ill. So long as he has a bed to lie on, a roof to cover him and some sensible person to look after him who will carry out the doctor's orders, he should be treated on the spot. Under war conditions this is of course not always possible, but the medical officer should always weigh the pros and cons most carefully before ordering a patient to be transferred to a hospital at any distance. It is better, when it can be arranged, for the nurse to go to the patient than for the patient to come to the nurse.

Baker and Dodds have shown that animals passing an alkaline urine are unaffected by injections of hæmoglobin, but if the urine is made acid, intra-renal obstruction follows. *In vitro* experiments show that hæmoglobin is precipitated when (1) the reaction of the solution is not more than about pH6, and (2) the NaCl content is about 1 per cent. or over. It appears, therefore, that hæmoglobin is excreted in the glomerular exudate, and that after concentration in the tubules the acidity and salt concentration increase, resulting in precipitation of the pigment.

Endeavour to produce an alkaline diuresis by administering alkalies, for example sodium bicarbonate, which may be given intravenously in a 2 per cent. solution (160 grains to the pint) in distilled water. One pint is injected, and this may be repeated an hour later, and subsequently if required, provided that there is no sign of œdema of the lungs. At the same time alkaline drinks should be taken in small sips; this may have the additional advantage of controlling the bilious vomiting.

If oral administration of alkalies is relied on alone, the doses should be large, and over 200 grains of sodium bicarbonate may be given in the twenty-four hours. The addition of an acid to urine containing sodium bicarbonate will cause an effervescence due to liberation of CO_2.

To combat the blood loss and to provide adequately functioning red cells to maintain the urinary secretion, blood transfusion has been found of the greatest value, especially in the polyuric type and in those showing repeated or continued hæmolysis; but it should not be undertaken in the presence of anuria. The blood used must be absolutely compatible and cross-matching is essential, since incompatibility itself produces hæmolysis and in severe hæmolytic states the red cells are prone to auto-agglutination. From 300 to 500 c.cm. of citrated blood are given, best as a straight transfusion, and repeated as required. Transfusion has no effect on the hæmolytic process and the transfused cells may be hæmolysed as readily as the patient's own. Its value lies in providing functioning red cells as required. Anti-coagulants are of little if any value.

Diuretics which stimulate the kidneys must be avoided. Sufficient flushing of the kidneys may be secured by administration of fluids by the mouth. In addition to the alkaline drinks already mentioned, the patient should be encouraged to take as much water, tea, barley-water or raisin tea (*see* p. 98) as possible. If this endeavour fails to accomplish its purpose, recourse may be had to saline injections. As an alternative to the intravenous infusion already described, saline may be given per rectum, six or eight ounces of physiological salt solution being administered if necessary every hour or even oftener. In mild cases enemata every four or six hours will suffice.

In very jaundiced cases where the liver is thrown out of action and there is a poisoning of the higher centres the patient becomes restless, watchful, excited, anxious and light-headed. He complains of severe headache, wanders in his mind and suffers from an incoherency of ideas and from hallucinations. His muscles twitch and tremble, and delirium, usually of a low muttering type, ensues. There may be convulsions and coma. In such cases the effect of glucose should be tried. Apart from the raisin tea already mentioned, solutions of glucose should be given as enemata or intravenously, 47 grammes of crystallized glucose to 1000 c.cm. of water. Intravenously 300 c.cm. of this solution which, as will be seen, is practically 5 per cent., may be given duly warmed and sterilized. Lactose can also be used in 10 per cent. solution.

As mentioned above, as soon as the stomach can tolerate food a fluid diet should be given in the form of whey, albumin water, milk, chicken broth and Benger's food. Raisin tea, on account of the sugar it contains and the fact that it is often well retained, is useful. In certain cases recourse may be had to rectal feeding. It is very necessary to guard the patient against chill to the kidneys, for nephritis is apt to follow blackwater and cases which recover from the latter sometimes die later from chronic Bright's disease.

Frequent sponging may be useful. If, despite alkalies, suppression threatens, wet or dry cupping and the application of poultices or hot fomentations to the loins can be tried.

The tendency to cardiac failure is best combated by strophanthus, digitalin or pituitary extract and the patient should not be allowed to sit up in bed. When vomiting is bad the stomach may with advantage be washed out with bicarbonate of soda solution. Ice, tincture of iodine (3–5 drops in a little water), sips of very hot water

or a dose of morphia, may check it, but probably the most effective treatment is champagne, iced if possible, taken in small sips. Constipation must be prevented.

For restlessness and pain in the back and legs morphia, hypodermically, is often invaluable, but it must be given cautiously and in small doses. Cold applications to the head and especially behind the ears alleviate headache. After an attack the patient is very weak and anæmic. He requires careful feeding and tonics, especially iron: as soon as the acute symptoms have ended, iron and ammonium citrate gr. 40 t.d.s. may suitably be prescribed. It is advisable that he should be invalided out of the endemic area, and he should be specially warned as to the danger of getting chilled or wet.

As quinine is often the " trigger that fires the gun " of blackwater fever it is better withheld. Mepacrine may be given cautiously to those showing parasites in the peripheral blood; and even when no parasites have been found, mepacrine treatment should be commenced a few days after hæmolysis has ceased.

Treatment may be summarized as follows:—

(1) Absolute rest in bed, even for the mildest cases; skilled and careful nursing.

(2) Do not move the patient if it can be avoided.

(3) Protect the kidneys by fluids and alkalies.

(4) Combat the anæmia by transfusion.

(5) Treat the malarial infection with mepacrine.

CEREBRO-SPINAL FEVER

Introduction.—Cerebro-spinal fever is an infectious disease of the central nervous system. It arises when the causative organism, the meningococcus, having invaded the blood stream attacks the meninges, the brain or spinal cord.

The disease is variously known as cerebrospinal fever, cerebrospinal meningitis, meningococcal meningitis, posterior basal meningitis, spotted fever.

In England the academic name for the meningococcus is the *Neisseria meningitidis*, whereas in America the term *Neisseria intracellularis* is employed. In view of the fact that the organism is by no means always seen within the leucocytes the English name is considered to be more truly descriptive.

The commonest site of infection with the meningococcus is the nasopharynx, where it may give rise to a rhinopharyngitis, but in most cases no visible lesion is evident. The organism may therefore be readily transferred from person to person through aerial projection of infected droplets and the infection may become widespread

throughout a community without, of necessity, giving rise to obvious disease.

Under certain conditions the organism may invade the blood stream of individuals and attack the central nervous system to give rise to cerebro-spinal fever. On occasions the nervous system escapes and the disease is restricted to a meningococcal septicæmia.

The factors that influence the invasion of the blood stream are still imperfectly understood, and although the invasion may be associated with changes in certain characteristics of the infecting strain of organism it is undoubtedly largely a matter of individual susceptibility. There is much evidence to suggest that this sucepti-bility is produced, or at any rate increased, by fatigue and recent infections of the upper respiratory passages.

Experience has shown that it is rare for a contact of a case to develop the disease. During periods when the incidence of the disease is generally increased, as many as 70 per cent. of the population may be found to be harbouring the meningococcus without showing evidence of disease and the very extensive investigations undertaken during the 1914–18 war pointed to the fact that almost every case of cerebro-spinal fever was contracted from healthy individuals harbouring the organism. Further work carried out since then has confirmed these observations.

Cerebro-spinal fever may occur in individuals of all ages, and of either sex, but young men lately transferred from civil to military life appear to be especially prone to attack.

Clinical Considerations

Incubation Period.—The incubation period is indefinite. It may sometimes be as short as twenty-four hours and may be extended to as long as ten days or even longer, but the common period appears to be between three and five days.

Signs and Symptoms.

(i) *Stage of Invasion.*—This may be very brief, lasting a few hours only, but may go on for a week or more. The onset is apt to be sudden with malaise, moderate headache, fever, perhaps vomiting and occasionally a petechial rash.

(ii) *Involvement of the Nervous System.*—As the brain and meninges become affected the headache becomes intense and intolerable. The drowsiness deepens and the patient can only be aroused with difficulty. Vomiting increases and there is pain and stiffness of the neck. Meningeal reactions may be presumed as soon as the neck stiffness is evident or Kernig's sign unequivocal.

Clinical Types.—The clinical picture of cerebro-spinal fever is very protean and may range from the mild abortive case to the very severe and rapidly fatal type. Although no clear-cut division can be made between the various types they are discussed for the sake of simplicity under three headings :—

(i) *Mild or abortive type* in which malaise, possibly some "pharyngitis," moderate headache and slight fever may be associated with some stiffness of the neck.

Spontaneous recovery may occur within seven to eight days and meningeal involvement may not be appreciated clinically. The true nature of the disease may only be demonstrated after the laboratory investigation of the cerebro-spinal fluid.

(ii) *Average Type.*—The temperature and pulse rate are very variable. A rash may or may not be seen; when noticeable it is generally petechial. Vomiting is the rule. Effusions into the joints, myalgia, twitchings or muscular spasms may all be seen. The headache, at first frontal, later becomes general and agonizing. The patient may be drowsy, stuporous, restless, delirious or may be extremely irritable and resent all interference. The eye and face muscles may be affected and deafness also is not uncommonly noted.

As the meningitis develops the patient settles into the characteristic decubitus, lying on the side with the back to the light, knees drawn up and neck extended. Unconsciousness and incontinence develop.

(iii) *The Very Severe or Fulminant Type.*—The attack may be so overwhelming that the patient may die within twenty-four or forty-eight hours, without headache or any signs of meningitis. There may be an extensive purpuric eruption, bleeding from mucous membranes and perhaps pain and collapse from a terminal hæmorrhage into the suprarenal medulla.

On the other hand the patient may die of an acute encephalitis with violent headache, vomiting, early coma, and only slight fever.

(iv) *Sub-acute Meningococcal Septicæmia with Meningitis.*—In some patients the signs and symptoms may be limited to a moderate fever with skin lesions, muscle and joint pains. Meningitis may only develop after many days, weeks or even months, or not at all. The skin lesions may be petechiæ, rose-red papules, large purpuric patches or painful and tender pinkish nodes. The condition may be continuous or intermittent, each attack being heralded by a rigor and a fresh crop of spots. The cerebro-spinal fluid may be normal, but meningococci can be cultivated from the blood during each recurrence.

Diagnosis.—Although a clinical diagnosis of cerebro-spinal fever may be presumed in the presence of the classical signs and symptoms, especially during an outbreak of the disease, the only accurate method of diagnosis is the demonstration of the meningococcus in the cerebro-spinal fluid.

The cerebro-spinal fluid is usually under increased pressure and on occasions markedly so, but the increase is not always obvious without a manometer reading. In the early stages of the infection the fluid may be clear, but in most established cases it is turbid or frankly purulent. Even where the fluid is clear to the naked eye there will be an increase in the cell count with the majority of the leucocytes of the polymorphonuclear variety and the sugar content less than normal.

A careful examination of suitably stained smears will usually demonstrate the presence of gram-negative intracellular diplococci, but on occasions they may be very difficult or impossible to find. In some very severe cases or in those patients whose condition is rapidly deteriorating the cerebro-spinal fluid may only show extra-cellularly placed meningococci.

The infecting organism may be cultivated from the cerebro-spinal fluid of untreated cases on almost every occasion, even when it cannot be demonstrated in direct preparations, and the true identity established by serological analysis.

At the same time blood cultures taken early on in the disease, in a large proportion of the cases, result in the recovery of the meningococcus. Patients suffering from chronic meningococcal septicæmia may also yield positive blood cultures during the early stage of the infection or at the beginning of a relapse, but repeated blood culture is often necessary before success is obtained.

In view, however, of the fact that a large proportion of the patients will have received sulphonamide therapy before culture of cerebro-spinal fluid or blood can be carried out the successful recovery of the meningococcus cannot be so readily assured as it was before the introduction of this group of drugs. In order to overcome the bacteriostatic effect of the sulphonamide derivatives the addition of para-amino-benzoic acid (5 mg. per 100 c.cm.) to the cerebro-spinal fluid or the blood culture medium is recommended.

During the early stages of cerebro-spinal fever meningococci can usually be recovered from the posterior nares and in the great proportion of the cases will be found to belong to the same serological group as those infecting the meninges. Whilst such findings may not be of absolute diagnostic value they are sufficiently constant to be of some significance.

Differential Diagnosis.—Although during the period of increased general incidence the early recognition of cerebro-spinal fever may be simple, it is well to remember that it is clinically impossible to differentiate with certainty between cerebro-spinal fever and any other form of pyogenic meningitis. Of other forms of meningitis, the tuberculous form usually has a slower onset, but acute benign choriomeningitis, meningitic forms of acute anterior poliomyelitis and encephalitis lethargica or post-vaccinal encephalitis may be mistaken for cerebro-spinal fever.

In the fulminant cases the patient may be quite unconscious when first seen. During an outbreak, the possibility of cerebro-spinal fever must always be considered in any unconscious patient unless there is a definite history that rules out such a possibility.

In differentiating meningococcal septicæmia clinically from other conditions, Influenza, Typhoid, Undulant fever, Miliary tuberculosis, Erythema nodosum, Subacute bacterial endocarditis, Rheumatic fever, Gonococcal septicæmia, Relapsing fever, Sleeping sickness and Heat-stroke may have to be considered.

Lumbar Puncture

The diagnosis of cerebro-spinal fever depends upon the demonstration of the meningococcus in the cerebro-spinal fluid withdrawn by lumbar puncture. This procedure may, at the same time, have an

immediate therapeutic value in relieving the intolerable headache, and possibly the vomiting also, induced by the increased tension of the fluid. The pressure of the fluid in a normal individual varies between 100–180 mm. of water, but in a developed case of cerebro-spinal fever may rise to as high as 300 mm. It is important, therefore, that decompression should be slow and to obviate the risks associated with a too rapid lowering of the pressure it is desirable to have a manometer attachment fitted to the lumbar puncture needle.

Anæsthesia.—Patients suffering from cerebro-spinal fever may be so stuporous that lumbar puncture may be undertaken without any form of anæsthesia; nevertheless numbers are fully conscious or so irritable that they resent such procedures. If the operation is to be carried out with ease and success it is essential to obtain adequate flexion of the spine and to ensure against sudden movements of the patient. In the majority of cases, therefore, some form of anæsthesia is an advantage.

It is usually sufficient to employ local anæsthesia in the form of an injection of 2 per cent. procaine and adrenaline in the operation area. General anæsthesia is employed much less frequently to-day than previously, but there are occasions, such as certain cases of delirium or where there is spasm of the extensor muscles, where it may be useful. An intravenous injection of pentothal sodium is suitable for this purpose. A general anæsthetic should be avoided, however, whenever possible.

Apparatus Required for Lumbar Puncture.—Standard lumbar puncture needles, with manometer and connecting rubber tubing, if available.

Sterile test-tubes plugged with cotton wool.
Iodine.
Swabs.
Adhesive strapping.
Sterile towels.

Technique of Lumbar Puncture.

Preliminaries.—Successful lumbar puncture is largely dependent on the patient being in the correct position. The patient should lie on his side on a reasonably flat bed with the trunk flexed so that the lumbar spine is convex backwards and not rotated. The buttocks should be moved to the edge of the bed, and the trunk, neck and knees well bent, with the shoulders and pelvis vertical. If the operation area is hairy it should be shaved, washed and dried. Having placed the patient in the correct position an assistant should ensure its maintenance by placing one arm round the shoulders and the other under the bent knees. The lower lumbar and upper sacral region is swabbed with iodine and one sterile towel is placed over the buttocks and another on the bed under the lower buttock.

If an anæsthetic is to be used this procedure is now carried out.

The operator's hands should be surgically clean and dry. The lumbar puncture needle and accessories should be removed from the sterilizer, drained of water, and allowed to dry as much as possible.

Operation.—The site for the insertion of the needle is now defined. The best point for this is in the middle line between the 3rd and 4th or 4th and 5th lumbar spinous processes. The 3rd to 4th space lies on a horizontal line joining the crests of the ilia. Having chosen the space that provides the larger gap the operator places the tip of his left index finger on the upper part of the lower spinous process and inserts the needle, with the stylet in position, into the lower part of the interspinous space in the middle line. The bevelled edge should be in the longitudinal axis of the spine in order to diminish the chance of cutting the fibres of the ligaments.

The needle should be pushed through the skin quickly and then slowly directed forwards and slightly upwards, feeling the way for any obstruction. If bony resistance is encountered it is withdrawn a little and directed somewhat higher. With experience the sense of touch will often tell when the needle has reached and pierced the ligamentum subflavum, some 5 cm. from the surface in an average adult. When the operator judges that this barrier has been passed it is advisable to remove the stylet and see whether C.S.F. runs out. It is well not to go too far, for the needle may easily enter the venous plexus in front of the spinal canal and thus contaminate the fluid with blood. A "dry tap," on the other hand, usually means that the theca surrounding the subarachnoid space has not been penetrated. It is possible, however, that other causes may be responsible.

When the fluid begins to flow, the manometer is attached to the lateral arm of the needle and the stylet is withdrawn. The fluid runs into the manometer and its pressure is read on the millimetre scale. (The patient if fully conscious should be told to breathe easily, for irregularities in respiration may raise the pressure.) If the pressure is above 100 mm., fluid is allowed to escape until it reaches that level—but never faster than a quick drip. Two samples of about 5 c.cm. each are then collected in sterile test-tubes for immediate despatch to the laboratory. It is important to obtain one specimen of cerebro-spinal fluid free from blood. On removing the needle, the opening in the skin is covered with cotton-wool and collodion or with elastic adhesive strapping.

After operation, the patient may rest on the back or on either side, as suits best, with a single pillow under his head. There is no need to raise the foot of the bed unless the cerebro-spinal fluid pressure is not increased.

Treatment

General Principles.—The specific remedies are, at the present time, almost entirely confined to drugs of the sulphonamide series. Their employment has not only been responsible for a marked reduction in the mortality, but has changed the general aspect of the disease.

The addition of specific serum therapy to chemotherapy does not appear to influence the course of the disease. If, for any reason the use of serum is considered advisable it should be given intravenously or intramuscularly and not into the theca. There is little evidence, however, of the value of such a procedure.

Success in treatment is dependent on the early recognition of the disease, and the prompt exhibition of a suitable sulphonamide drug

in the correct dosage in order to obtain the optimum concentration in the blood and cerebro-spinal fluid without delay. This concentration should be maintained for the first three days and a somewhat lower level for the next five or six days.

In order to obtain the maximum effect of these drugs and to maintain the blood concentration at a desired level it is necessary to administer the drug at regularly spaced intervals throughout the twenty-four hours. Even in the case of patients asleep it is more important to wake them to administer their tablets than to allow them to sleep on and miss their treatment.

There are four sulphonamide derivatives the value of which in the treatment of cerebro-spinal fever has been substantiated. They are sulphanilamide, sulphapyridine, sulphathiazole and sulphadiazine.

Sulphanilamide is perhaps the least active against meningococci and the most likely to induce drug fever, rashes and later blood changes, but it seldom causes vomiting, depression or hæmaturia.

Sulphapyridine is less toxic and more effective, but causes nausea and vomiting and the patient tends to feel miserable or confused. The vomiting may prevent absorption of the drug.

Sulphathiazole is at least as active against the meningococcus as sulphapyridine and it is much less liable to cause vomiting or depression, but it is not always available at present.

Sulphadiazine would appear to be the most suitable and the least toxic of the four drugs. It is as active as sulphapyridine and sulphathiazole against meningococci, pneumococci and streptococci and almost the equal of sulphathiazole against staphylococci. Sulphadiazine has the added advantage of producing, with the same dosage, a more sustained higher average blood level than the other derivatives. At the present time, however, supplies are strictly limited and the drug is not available for general issue.

Fluid intake to promote a free urinary output is a most important adjunct of the treatment with the sulphonamide drugs. There is a tendency for these drugs to crystallize out in concentrated urines. It is recommended that so long as the administration continues the intake of fluids should be at least four pints a day for adults and sufficient alkalies should be added to render the urine distinctly alkaline (*see* also p. 74 under Hæmaturia and Anuria).

Adequate treatment should result in a minimum blood concentration of 5 mg. per 100 c.cm. within 4–6 hours of the administration of the drugs. Whenever there are laboratory facilities for the estimation of sulphonamide concentrations in the blood it is desirable that this should be carried out. The actual blood concentration with any given dosage is to a large extent dependent on the particular sulphonamide derivative employed, but variations in individual response are also important. It may, therefore, be necessary to increase the dosage of the particular sulphonamide employed or to change to another derivative in order to produce the desired blood concentration. Whenever this is carried out the blood level should be checked within twelve hours of the change in treatment. The estimation of the cerebro-spinal fluid concentration of the drug is of less importance, but should a subsequent lumbar puncture become necessary for the relief of tension opportunity should be taken,

where facilities exist, for this to be carried out. Repeated lumbar puncture should never be employed as a routine during sulphonamide therapy, and it is seldom indicated as a special therapeutic measure.

Regular evacuation of the bowels should be encouraged, but drastic purging should be avoided and if artificial means are necessary a simple enema should be administered on alternate days.

In the great majority of cases the most satisfactory method of exhibition of the sulphonamide drugs is by oral administration. They may be given in whole tablet form, or powdered and mixed with a little milk or dissolved in two or three ounces of 1 per cent. of hot citric acid in water. If a case presents difficulty in swallowing the drug may be administered as a dilute suspension through a nasal tube. It may often be an advantage to divide the doses and increase their frequency.

There are patients in whom for various reasons, it may be impossible to obtain a satisfactory blood level of the drug by oral administration. There are others, the victims of a fulminating infection or those in whom treatment has been delayed, where an immediate and adequate blood concentration of the drug is the only hope of saving life. In such cases intravenous or intramuscular medication is the only method of administration that is feasible. When the intramuscular route is employed special care should be taken to give the injection into the upper and outer quadrant of the buttock in order to avoid accidental damage to the sciatic nerve. The soluble sodium salts of sulphapyridine, sulphathiozole or sulphadiazine are suitable for this purpose. These soluble preparations, however, are strongly alkaline and intramuscular injections should only be employed in cases of urgency as they cause necrosis. Sodium sulphapyridine—the drug commonly used in this country—is in the form of a 33 per cent. solution and 3 c.cm. represents 1 gramme of sulphapyridine. Intravenous injections of the preparation diluted with three or four volumes of sterile freshly distilled water are to be preferred to the intramuscular route, but either method should be reserved for emergency or special use. Oral administration should be instituted or reinstituted at the earliest possible moment—if practicable at the same time as, or immediately after, the injection.

Treatment should be commenced immediately there is reasonable evidence pointing to infection of the meninges and should not be delayed until the diagnosis has been established by lumbar puncture.

Cases of ordinary severity should be treated wherever seen with oral administration of sulphapyridine. Very severe or fulminant cases should receive intravenous or intramuscular sulphapyridine-soluble whenever possible and arrangements made for their immediate admission to hospital.

It is essential, however, that whenever patients receive preliminary treatment with sulphonamide drugs outside hospital or when they are transferred from one hospital to another, the name of the preparation, the dosage, the route and the time of administration must be accurately noted and forwarded with the patient.

Routine Treatment.—The standard routine treatment, based on the present availability of the various sulphonamide derivatives.

of the mild and moderately severe types of cases consists in the oral administration of sulphapyridine tablets.

The total dosage during twenty-four hours should be 8 g. and in extreme cases up to a maximum of 10 g. The spacing of the dosage is important. The compound should be given four-hourly night and day. In order that the maximum effect of the drug can be obtained as early as possible the initial administrations should be relatively larger than the maintenance doses and the following table gives the standard dosage recommended :—

Initial dose	2·0 g.
4 hours later	2·0 g.
8 ,, ,, ...	1·0 g.
12 ,, ,, ...	1·0 g.
16 ,, ,, ...	1·0 g.
20 ,, ,, ...	1·0 g.

Continue with 1·0 g. four-hourly for the next 36–48 hours, after which the dose should be reduced to 1·0 g. eight-hourly for the next six days. To prevent recurrence of infection the administration should continue for some days after the disappearance of clinical symptoms. Normally the total period of sulphonamide treatment should not exceed nine days.

Treatment of Special Cases.

(i) *Cases in which Treatment has been Delayed.*—With cases which have an onset so insidious that their nature is not recognized until late in the course of the disease it is essential to lose no time in ensuring the absorption of the drug. Whenever there is a suspicion that there has been delay in recognizing the condition, whether the patient is conscious or unconscious, the first dose should be an intravenous injection of Sulphapyridine Soluble. As soon as meningeal involvement is suspected the injection must be given. It must not be delayed until the case is admitted to hospital or lumbar puncture performed. The suggested scheme for the administration of the drug in these cases is as follows : Whether conscious or unconscious, the first dose should be 1 g. (=3 c.cm.) Sulphapyridine Soluble by intravenous injection, diluted in three or more volumes of saline. If unconscious, subsequent doses should be four-hourly injections of 1 g. Sulphapyridine Soluble. If conscious and able to swallow, administer 1 g. of sulphapyridine in tablet form or crushed and dissolved in 100 c.cm. of hot citric acid solution (1 per cent.) by the mouth two hours after the injection, and then 2 g. by the mouth four hours later. (This represents approximately half the total twenty-our-hour dose.) There after proceed with ordinary routine treatment.

(ii) *Fulminating Cases.*—The onset may be extremely rapid, and it is essential, therefore, that the optimum blood concentration of the drug should be attained at the earliest possible moment. The first dose should consist of two injections given simultaneously : an intravenous injection of 1 g. Sulphapyridine Soluble, diluted in three or more volumes of saline, and an intramuscular injection of 1 g. Sulphapyridine Soluble. The second dose should be an intravenous injection of 1 g. Sulphapyridine Soluble four hours later.

Subsequent doses must be judged by the condition of the patient, but oral administration of the drug should replace the intravenous

or intramuscular route as soon as is practicable. Dosage may be continued according to the scheme given above for cases of delayed diagnosis and treatment. Three or four pints of fluid daily should be given by whatever route is practicable, either oral, rectal, subcutaneous or intravenous.

(iii) *Septicæmia without Meningitis.*—The same course of treatment should be applied to any case of meningococcal septicæmia whether meningo-encephalitis has developed or not, that is to say, sulphapyridine in doses of 2 g. is administered at four-hourly intervals for the first eight hours and then 1 g. four-hourly for the next forty-eight hours when the dose may be reduced to 1 g. eight-hourly for a further period of six to seven days.

Nursing of Cases.—The nursing of cases often makes heavy demands on the staff of hospitals and successful treatment depends on skilful and tireless attention. Tact, firmness and patience are needed to ensure that during delirium or stupor the patient takes the fluids and the medicines prescribed. This is especially important at night time when it is essential that patients should be given the medicine at the prescribed time and not allowed to miss a dose because they are sleeping.

A high standard of nursing discipline is required so that instructions regarding the dosage, the spacing of the doses and the administration of sulphonamide drugs and fluids are faithfully followed and accurately recorded on the temperature chart.

Treatment of Special Symptoms.

Unconsciousness.—When consciousness is impaired medication by the mouth may be impossible. Nevertheless it may be possible to induce automatic swallowing of a suspension of sulphonamide by the gentle administration of the preparation, a spoonful at a time. When this method is not practicable there remains intravenous therapy or the introduction of the drug through a nasal tube. Whilst an adequate swallowing reflex remains fluids may be administered through a nasal catheter passed as far as the back of the pharynx ; should the swallowing reflex be abolished the same method may be utilized provided the catheter is passed into the œsophagus. It should be noted that thick suspension may easily block the catheter, and it is therefore necessary to wash-through the tube with adequate amounts of clear fluids.

Vomiting.—In the early stages vomiting will be due to the disease itself, and it may be impossible to obtain an adequate blood concentration of the drug by oral administration. The only satisfactory method of exhibiting the drug in such cases is by the intravenous injection of the soluble sodium salt for the first two or three doses, after which the disease should be responding to treatment and vomiting due to this cause should have ceased. Sulphapyridine, however, is of itself a cause of vomiting and, if splitting the dosage and increasing the frequency of administration either by the normal oral route and via a nasal catheter still results in vomiting, it may be necessary to change to another sulphonamide derivative. If sulphathiazole or sulphadiazine is available these are the drugs of

choice ; otherwise sulphanilamide should be substituted. Sulphanilamide rarely causes nausea or vomiting, but it is less effective against the meningococcus than the others mentioned.

Restlessness.—Quiet, a darkened room, and skilful nursing are often more effective than sedatives. Nevertheless there are occasions when bromides, chloral or even rectal or intramuscular administrations of paraldehyde are indicated. Some patients may require an injection of morphia (gr. $\frac{1}{6}$) to tide them over an excitable period before chemotherapy can be effective.

Headache.—The diagnostic lumbar puncture and the sulphonamides usually reduce the intolerable headache dramatically. In the cases where the violent headache persists it may be necessary to repeat lumbar puncture, but rarely is such a procedure required.

Incontinence.—When consciousness is impaired the bladder should be emptied by catheter every six hours if the patient fails to pass urine involuntarily or reflexly. The likelihood or frequency of incontinence of the fæces will be lessened by routine enemas. When control of bladder or bowel is lost especial care should be paid to the cleansing and drying of the skin.

Toxic effects of Sulphonamide Derivatives

Whilst there are certain side-effects that are more or less peculiar to a particular derivative there are others that are common to the whole group.

Granulocytopenia.—Although this toxic effect is rare it is a danger that must be considered whenever drugs of this group are being administered, especially when the period of administration extends beyond seven or eight days. As a precautionary measure a total and differential white blood cell count should always be undertaken in those cases in which the administration of the sulphonamides is considered to be advisable beyond this period. The leucocyte count should be carried out at an earlier stage if a patient, originally responding to treatment, begins to go downhill or if any sign suggestive of agranulocytosis develops.

More commonly granulocytopenia develops during sulphonamide therapy after the patient has responded to the pharmacological action of the drug. The onset of the condition may then be recognized by vague symptoms of lassitude, malaise, muscular pains, fever with soreness of the mouth and throat. In those cases where the condition develops whilst there are still residual symptoms of the primary disease the onset of granulocytopenia may be extremely difficult to appreciate clinically and can only be diagnosed by the blood picture.

Unless prompt action is taken the condition progresses rapidly. The first indication of agranulocytosis demands immediate withdrawal of the drug, free administration of fluids and treatment of the condition with pentose nucleotide. In severe cases 20 c.cm. should be given by intramuscular injection once or twice daily for three or four days and the dose gradually reduced as the blood picture improves. Whole-blood transfusions may prove of benefit.

Whenever there is a history of previous sensitiveness to sulphonamides, especially with regard to a granulocytopenia, drugs of this group are contra-indicated.

Hæmaturia and Anuria.—During the administration of sulphonamides there is a tendency, especially in the case of sulphapyridine, for the drug to crystallize out in acid concentrated urines. This crystallization may take place within the renal tubules, renal pelvis or ureters and so block the outflow of urine leading eventually to anuria. The immediate withdrawal of the drug and the rapid flooding of the kidney by copious alkaline drinks, may lead to complete recovery if the signs are noted sufficiently early. The conditions may develop very rapidly and backward washing by ureteric catheterization or even nephrostomy may fail to free the blockage.

Prophylaxis depends upon the free administration of fluids. When a patient is receiving 6 g. of sulphapyridine in twenty-four hours at least four pints of alkaline fluids should be taken. If this dosage is exceeded considerably greater fluid intake is necessary. Experience of this condition indicates that the bulk of the fluid intake is more important than its alkalinization.

The urinary output of each patient should be measured daily. The urine should also be examined for the presence of crystals of the drug after standing at room temperature for some hours. The deposition of crystals in the voided urine may be the first indication of this complication and prompt action may avert a serious result.

Cyanosis.—Cyanosis may appear during the course of treatment. It is especially liable to occur if sulphanilamide is employed and is due to methæmoglobinæmia or sulphæmoglobinæmia. In patients already debilitated by an illness, not previously treated with sulphonamides, it may be advisable to exhibit methylene blue orally in doses of 0·5 to 1·0 g. Generally, however, the condition may be safely ignored.

Drug Fever and Drug Rashes.—Both these conditions are more frequently associated with sulphanilamide than other derivatives.

Fever due to the drug may be recognized in a patient who has initially responded to treatment, but in whom a rise in temperature up to 101° F. is noted about the 8th day. Prolonged treatment with sulphanilamide may also be responsible for drug fever.

Rashes, frequently morbilliform types, may accompany the fever or may occur independently. Both drug fever or rash portend more serious evidence of toxicity and daily leucocyte counts should be instituted immediately such signs are encountered and continued for at least a week from their appearance.

Nausea and Vomiting.—These effects have already been mentioned.

Mental and Nervous Conditions.—The depression and miserableness induced by sulphapyridine are very real and common experiences of patients treated with this derivative, but other mental symptoms ranging from dullness to delusions are occasionally noted during the administration of other sulphonamide drugs.

Prognosis

Cerebro-spinal fever must always be regarded as a grave disease for, in the absence of early and adequate treatment, the mortality is extremely high. Nevertheless, apart from the fulminant types and certain rare complications, early treatment with sulphonamides in the correct dosage has greatly reduced the mortality.

Prevention

Experience has shown that it is rare for cerebro-spinal fever to be spread by patients actually suffering from the disease. When two or three cases occur in a group of individuals in contact with each other the evidence suggests that the disease is contracted from those harbouring the meningococcus, but who are not suffering from cerebro-spinal fever.

Nevertheless the patient is, theoretically, a source of infection and should therefore be, if possible, isolated. The first practical step in prevention is the early diagnosis and treatment of the disease as it occurs. The medical officer who makes a clinical diagnosis of cerebro-spinal fever should take action in the following order of priority :—

(1) Make arrangements for the immediate treatment of the patient as outlined on p. 71, and also for the admission of the patient to hospital. If no isolation hospital is close at hand the patient should be admitted to the nearest military or civilian hospital with good facilities for treatment, nursing and laboratory investigations.

(2) Ensure that full records of the case together with a note of the remedies given, dosage and times of administration accompany the patient to hospital.

(3) Make arrangements for the disinfection of clothing, bedding and any articles that may have been soiled by discharges from the patient's nose or mouth. The meningococcus is a delicate organism and does not remain viable outside the body for any length of time and it is sufficient to wash the floor and furniture in the vicinity of the bed with soapy water.

(4) The medical officer who diagnoses the case is responsible for its notification on A.F. A 35 (notification of infectious diseases), which should be completed in all detail. The original will be retained as an office record. A copy will be forwarded through the usual channels to D.D.M.S. command or corps, or the A.D.M.S. of area district or division, whichever formation is immediately responsible for the unit with which the patient served. A copy will also be sent to the officer in medical charge of the effective troops or military families concerned. Should the diagnosis be made by either of these officers a copy will be sent to the military hospital receiving the patient, if the case was admitted to this type of hospital. In addition the local civil health authorities will be informed.

Officers in medical charge of effective troops amongst whom the patient served are responsible for the health of the remaining troops, and they should take the earliest steps to investigate conditions associated with any outbreak.

A contact is one who is a close personal associate of a patient suffering from cerebro-spinal fever. Such individuals are not more likely to develop the diease than those who are not contacts and they should, therefore, not be isolated. It is, however, advisable to note contacts for observation purposes. That is to say, medical officers should see all individuals who were in close association with the patient at least once daily for ten days in order to be assured that they are in good health. This precaution is advisable, not because the associates are likely to have been infected by the patient, but because these individuals, owing to their association, might have become infected from a common source.

There is no specific remedy known at present that is effective as a prophylactic measure. There is no valid evidence to show that preventive inoculation or gargling has any prophylactic value. Sulphonamides are sometimes given as prophylactics, but it should be noted that these drugs may not be effective in the dosage advised, and may produce drug-fastness or masking of symptoms. They cannot, therefore, be recommended.

General Preventive Measures.—Meningococcal infections may be conveyed from person to person by naso-pharyngeal discharges ejected from the nose and mouth of patients suffering from cerebro-spinal fever or meningococcal rhino-pharyngitis or healthy carriers. Cross-infection may be direct at close range from mouth to mouth or may be air-borne over distances of 20 to 30 feet in the case of the finer droplets. Close-range infection may occur in the open air or within buildings, but it is probable that the finer droplets cause infections only within buildings.

From available evidence it would appear that the healthy carrier or the individual with a meningococcal rhino-pharyngitis is the main source from which the infection is spread.

Although the carrier rate may be high during an outbreak this is not invariably so. Post-nasal swabbing, for the estimation of the carrier rate, of large groups of individuals has been found to serve no useful purpose in controlling the incidence of the disease and should not be carried out. Post-nasal swabbing should be restricted to special investigations recommended by the consulting physician.

During periods in which the general incidence of the disease is raised it is important to observe any measure that may contribute towards lessening the chance of infection and increase the chance of recovery of those individuals who contract the disease.

Early Recognition.—Medical officers should give short talks to regimental officers and senior N.C.Os. on the disease and the method of spread. They should, above all, encourage all ranks to report "sick" immediately if they are suffering from headache, soreness of the throat, etc. Furthermore, their interest should be enlisted in the further hygienic measures outlined below.

Overcrowding.—Although cerebro-spinal fever may be justly regarded as a disease associated with institutional life the original

view that the increased incidence was due to overcrowded dormitories has not been fully substantiated in the light of present knowledge. That overcrowding is a most important factor in the spread of the disease is, in all probability, correct. But however generous may be the spacing out of beds, as long as individuals are crowded together at narrow tables in lecture rooms, dining halls, etc., so long will ideal conditions exist for the transfer of the organism from one nasopharynx to another.

In sleeping quarters the minimum distance allowed, in war time, between the centres of beds is 5 feet. Should it be necessary to reduce the space to this minimum every alternate bed should be turned round so that each man sleeps next to his neighbour's feet.

The most dangerous periods in dormitories are during the going-to-bed and getting-up times. Unless a number of the occupants are suffering from coughs the projection of infected droplets is much less during sleep.

Ventilation.—All occupied rooms, including barrack rooms, institutes, dining-rooms, lecture rooms, etc., should at all times be so ventilated that there is a free circulation of air. But unless there is adequate heating this recommendation will not be followed. As the maximum intensity of the occupation of buildings by the soldier occurs during the black-out time in winter particular attention must be paid to the provision of a sufficiency of efficient ventilator openings.

The provision of adequate ventilation without contravening blackout regulations may not be an easy matter in some buildings, but it is the duty of all C.Os. to make every effort to see that the best ventilation possible is obtained in every occupied room. In order to ensure that satisfactory ventilation is maintained constant inspection by officers or senior N.C.Os. is necessary.

For military reasons, unless there is an adequate safeguard to prevent the switching on of lights, the removal of black-out screens to effect better ventilation is not recommended. Efficient heating of occupied buildings or an adequate supply of blankets for the beds during the cold weather is essential, otherwise all efforts to maintain satisfactory ventilation will be circumvented.

Outdoor Life.—Meningococcal infections are most readily transmitted when people are crowded together in ill-ventilated rooms. It is, therefore, important that all ranks, and especially those recruits under training, should spend as much of their day as possible in the open air. At the same time, it must be remembered that over-fatigue and long periods without hot meals should be avoided, as young recruits may thus become liable to colds and other minor disabilities that may render them susceptible to a blood-stream invasion of the meningococcus, should this organism reach the nasopharynx.

Sequelæ, and their Treatment

Focal nervous symptoms developing during the course of the disease are not common and most of them are transient. They include cranial nerve palsies, for example, of the 3rd, 6th, 7th or 8th, visual

impairment, epileptiform seizures, aphasia, monoplegia or hemiplegia of cerebral origin, paraplegia from myelitis, and atrophic palsies with or without sensory loss due to spinal root lesions. Some degree of weakness from hemiplegia, paraplegia or spinal root involvement may persist, but improvement tends to continue for months. Deafness, of varying severity, unilateral or bilateral, from neuritis of the auditory nerve is frequently, but not invariably, permanent. It occurs in about 5 per cent. of cases.

General nervous symptoms are more frequent, a fact which has only recently become recognized. The highest proportion of cases occur in the age periods between fifteen and forty-five, and rather more often in males than in females. In the complete syndrome the complaints are of headache, giddiness, minor mental and emotional disturbances, alteration in personality, insomnia and fatiguability, a clinical picture which closely resembles that which often follows head injury. The basis of it, from whichever cause, is organic cerebral damage, but it is often complicated and perpetuated by psychogenic factors resulting from anxiety, an appreciation of change in physical and mental state or a desire to use invalidism for selfish ends. Such psychological complications are more liable to develop in those with a previous history of unstable temperament and neurotic illness.

Up to the present experience has shown that recovery is, in the majority of cases, to be expected, but it is believed that results would improve if the conditions were early recognized and convalescence were suitably planned. At the important stage when the patient is still in hospital points of practical value have to be kept in mind by the medical officer.

(i) Headache, giddiness, fatiguability and other symptoms of the syndrome, as in the case of head injury, may be absent so long as the patient is in bed or even under the restricted conditions of ordinary hospital life. They may appear only when more normal activities are attempted. For this reason, before patients are discharged from hospital and their immediate disposal decided, their mental, emotional and physical stamina should be tested unobtrusively. Thus, their response to reading, noise, the cinema, games and other forms of exercise should be investigated.

(ii) Since the symptoms are subjective and usually unsupported by physical signs it is essential that the medical officer should not only be familiar with the clinical picture, but should inquire, so far as possible, into the patient's previous history in regard to neurotic illnesses and work record, as well as present anxieties and keenness and efficiency as a soldier. Care must be taken during the inquiry not to suggest symptoms.

(iii If symptoms which constitute real disabilities are neglected and the patient is prematurely sent back to duty, worry and resentment may well develop and delay or prevent recovery.

Those patients who, at the end of two or at most three weeks' convalescence in hospital, still complain of disabling symptoms

should be sent to convalescent homes where active rehabilitation can be provided. An aimless convalescence should never be allowed, for it would foster laziness and neurosis and sap the will to get well.

This group of cases which, in their symptoms so closely resemble the common sequelæ of closed head injuries, present a problem which tests the clinical judgment of the medical officer. For whilst the symptoms which have been described are primarily due to structural damage, and in their main features can be recognized by those familiar with them, the picture is often blurred by a neurotic or even conscious bias determined by the psychological background, present difficulties and desires, as well as by suggestions from companions, relatives or careless history-taking. The medical officer must, therefore, be watchful neither to neglect the possibility of such sequelæ nor to be obsessed by them. He must, in fact, evaluate the whole situation in each case on the available evidence and it will often be necessary to take some trouble to get it.

Further investigation into the frequency, treatment and prognosis of nervous sequelæ of cerebro-spinal fever in soldiers is necessary, and for this purpose all patients before they leave hospital should be examined by a neurological or medical specialist and ophthalmologist, who will decide whether special rehabilitation treatment in a convalescent home is necessary and will again, after re-examination, advise by written report on final disposal.

Stiff joints from arthritis, in meningococcal septicæmia, can usually be overcome by physiotherapy.

CHOLERA

Cholera is endemic in many parts of the East and has been known in India since the earliest times. The disease may be spread by human agency from any of these foci in epidemic form. Sporadic cases due to carriers may occur anywhere, but a community under good sanitary control need never fear an extensive spread of cholera. Rogers has shown that cholera does not spread in epidemic form in India if the absolute humidity (the weight of the aqueous vapour in the air measured in terms of its mercury tension) is not above 0·400.

Etiology.—Cholera is caused by the comma-shaped, single-ciliated, Gram-negative vibrio of Koch, which lives, multiplies and produces an endotoxin in the small intestine. Acton and Chopra state that the main actions of the toxic bases of cholera toxin are :—

(1) A fall of blood pressure due to dilatation of the vessels supplying the small intestine, combined with an increased permeability of the vessel endothelium ; (2) Direct damage to the secreting tubules of the kidneys which are further hampered by the occurrence of an intertubular œdema as soon as the blood pressure has again risen to normal.

Research work has shown that under war conditions the cholera "carrier" is undoubtedly the most important factor in spreading

infection, but the rôle of water, food, fomites, flies and faulty conservancy methods must also be kept in mind. Vibrios have been found in the fæces of flies for twenty-four to thirty-six hours after ingestion of infected material by the insects.

Cholera vibrios often disappear from the fæces of patients in three or four days and rarely persist in them for longer than twenty days, but the healthy cholera carrier may go on passing vibrios for a period of two months or longer, a gall-bladder infection having become established. As a rule, however, the carrier only excretes vibrios for a week or ten days. An attack of diarrhœa or the administration of a purgative will often cause vibrios to appear in the stools of a carrier case and a purge may even excite an attack of cholera in a carrier. In India cholera vibrios have been known to live as long as seventeen days in stools kept in the dark and with evaporation prevented. The average time of survival is shorter in hot weather—in June one to two days, in February seven days (Greig).

Symptoms.—Incubation period: a few hours to six, or even more, days. Stages: those of Evacuation, Algidity and Reaction. In a certain number of cases there is a premonitory diarrhœa, which is probably catarrhal in nature and may predispose to the choleraic attack. In other cases the *stage of evacuation* commences suddenly with profuse and frequent motions which may or may not be associated with colic. Indeed a sense of relief may accompany the passage of the stool. The attack is usually nocturnal. The motions, at first fæculent and bile-stained, quickly assume the typical rice-water appearance, there being small white flocculi of intestinal epithelium in a slightly opaque fluid. Pints of this material may pour from the patient, who rapidly becomes prostrated. He begins to vomit, and suffers greatly from thirst. The vomited matter, which consists at first of food, soon changes to rice-water fluid, and gushing from the mouth is apt to contaminate attendants. Cramps of the legs and abdomen set in, the tissues shrink, the eyes become sunken, the nose pinched, the skin cold and dusky or earthy in hue, the pulse feebler and the urine less. In the initial stages the brilliant white, pearly colour of the eyelids, especially of the lower lid, makes the eyes appear large and bright. Hiccup may be obstinate and persistent.

Algid Stage.—The serious symptoms become intensified, the skin of the fingers shrivels (washerwoman's fingers) and the nails may become black. The eyes are sunken. The voice is husky. The body surface is cold, livid and bedewed with a clammy sweat. There may be cyanosis, general or localized, and sometimes this is so intense in the lower extremities as to simulate gangrene. The pulse at the wrist may almost vanish, and if a vein be incised only a drop of black and tarry blood may slowly exude. This concentrated blood, which has been likened to currant jelly, has a specific gravity of 1,072 to 1,078. The kidneys cease to act. The patient is restless, very thirsty, and may or may not continue to be racked by cramps. While the surface temperature is low that of the rectum is often elevated.

The mind is clear but the patient is apathetic. In fatal cases and usually some ten to twelve hours after the beginning of the

attack coma supervenes, leading to death, but fatal collapse may occur much earlier or much later. The algid stage may terminate in recovery, the pulse returning at the wrist, the skin becoming warm, urine being secreted and convalescence established in a short time. More frequently the patient enters upon the—

Stage of Reaction.—The favourable symptoms just mentioned appear and continue, the motions diminish and now contain bile. At the same time a febrile condition manifests itself, of which the sole indication may be a bloodshot state of the eyes. The febrile manifestation may be slight or severe, and in the latter case a hyperpyrexial condition may ensue. During this stage of reaction the patient may die from pneumonia, enteritis, diarrhœa, hyperpyrexia or uræmic poisoning. Abortive and typhoidal reaction stages are described, and in the latter the pyrexia may last as long as a fortnight.

Such is a picture of cholera gravis, but on the one hand mild ambulant cases occur where the carrier is a special danger, and on the other there is fulminating cholera in which toxæmia causes rapid death before vomiting or diarrhœa have time to set in. Of this nature is the so-called cholera sicca apt to occur amongst debilitated troops. In one of the Balkan wars rice-water stools were sometimes absent even in severe cases of cholera. It is worthy of note that rashes of various types may occur in cholera, usually during the stage of reaction.

Diagnosis.—It is beyond the scope of this section to deal with the bacteriological diagnosis of cholera, but it is well to remind the medical officer that in the case of suspected carriers who are constipated, rectal swabs should be sent to the nearest laboratory, while in the case of an autopsy on a suspected case of cholera two 5-inch sections of the small intestine, one taken just above the ileocæcal valve and the other from the middle of the ileum, should be cut out after double ligaturing, placed in sterile, well-stoppered bottles and submitted to the bacteriologist as quickly as possible. If culture media are available an agar or blood serum slant should be made from the material at the same time, as the vibrios are apt to be killed by the fæcal bacteria.

Differential Diagnosis.—Many cases of cholera in the late Balkan war were diagnosed as bacillary dysentery, and it must be remembered that the serous form of the latter may closely simulate cholera. Further, recent work has shown that amœbic dysentery may sometimes do likewise. It is said that if dysentery coexists with cholera, cramps and rice-water stools may be absent. It should be remembered that dysentery, typhoid and paratyphoid may coexist with cholera and there may be no sign of the concomitant disease till the cholera is over. There is a form of pernicious malaria which presents choleraic symptoms, but the high axillary temperature should help to distinguish it from cholera.

Severe diarrhœa of the cholera nostras form, food and mushroom poisoning, irritant metallic poisoning and the early stages of trichinosis need merely be mentioned. Note that in food poisoning the vomiting usually *precedes* the diarrhœa.

Complications.—Of these gangrene and pneumonia may be mentioned, but remember that intense local cyanosis may be mistaken for gangrene.

Prophylaxis—Personal.—Anti-cholera inoculations are now practised. These seem not only to give a considerable degree of protection but to lessen the risk of a fatal issue in the inoculated. The dose should be at least 12,000 million bacilli given in two inoculations at seven or ten days' interval. The local reaction is very slight and there is rarely any general disturbance. The duration of the immunity produced does not seem to be great and the inoculation should be repeated after the lapse of four months.

Although some condemn the practice as being apt to upset the stomach, the use of lactic acid in tea or the addition of vinegar or of 30 drops of dilute hydrochloric acid to every pint of drinking water has much to commend it. The last method has been used in India, to all appearance with great success. Ten-drop doses of eucalyptus oil given twice daily have been strongly recommended. Give in mucilage and syrup of lemons.

When possible all indigestible diet should be avoided. Special care is needed as regards fruit, raw vegetables and meat jellies. Lettuces and celery being moist and eaten uncooked are specially dangerous. Vibrios have been found to survive on lettuce leaves for twenty-nine days. Melons and cucumbers must be avoided, as they are often perforated and steeped in water to increase their weight.

Those who handle patients or corpses should wear indiarubber gloves, and doctors, nurses and orderlies should be provided with overalls and gum-boots. Nothing should be conveyed to the mouths of attendants in a cholera ward. The careful disinfection of the hands coupled with the use of a stout nailbrush is very important. The practice of hand-shaking should be discouraged during cholera epidemics.

Prophylaxis—General.—Cholera patients must be isolated for forty-two days or until three successive daily stools obtained after the administration of a cholagogue have been proved negative as regards pathogenic vibrios. Cholera stools should be disinfected by adding an equal amount of a 5 per cent. cresol solution and allowing it to remain in contact with the stool for at least one hour. Fresh chlorinated lime (1 lb. to 4 gallons) may be used in the same way. Roughly, two tablespoons to the pint of cholera dejecta are required. Nothing is better than quicklime if it can be obtained. Add together equal parts of fresh quicklime and water, and then dilute with three times as much water as previously used. Add a quantity of this mixture equal to the amount of stool to be disinfected and allow it to remain in contact for one hour. When ground has been fouled by dejecta or vomit disinfection may be carried out with cresol, or by raking hot ashes over it or by pouring kerosene over it and setting the kerosene alight. Cholera-soiled clothing, bed linen, and blankets should be stoved or soaked in 2½ per cent. cresol solution.

Contacts should be isolated and kept under surveillance for five

days while carriers should be sought for, particularly amongst those handling food in any way and those suffering from diarrhœa. Established carriers should be quarantined until the stools are negative, usually for three to four weeks. As regards carriers, it must be remembered that the use of purgatives may induce an attack of cholera.

Cholera is very often water-borne and it is essential that the strictest supervision be maintained over all water supplies. Drinking water should be carefully chlorinated, or, if this is impossible, boiled, whilst precautions must be taken to guard against subsequent contamination. Water bottles should be disinfected with boiling water or strong bleach solution, or potassium permanganate solution. The latter is also used for the disinfection of wells, washing of hands, and for many other purposes as it has a specially destructive action on the vibrio of cholera. Ghurras, water chatties, and massacks are often the source of infected water and should receive attention. Wells should be policed and properly supervised. Bathing in ponds and pools should be prohibited, and established bathing places will require inspection and regulation.

All milk should be boiled and the sale and consumption of uncooked fresh fruit and vegetables forbidden.

All dish-cloths and cooking utensils should be boiled and special attention paid to the cleanliness of cookhouses.

Finally, anti-fly measures must be redoubled and cresol solution used in all latrines in which adequate fly-proofing is not in existence.

Treatment.—For the most part drugs are of little use in cholera. The Indian practice is to treat the premonitory diarrhœa by giving half an ounce of castor oil with a tea-spoonful of brandy. This is probably wise, as it clears the bowel of irritating material.

Even in the mildest cases absolute rest in bed is essential, a warmed bedpan being provided. No food is to be given while the disease is active. The surface of the body must be kept warm. Hot sandbags to the body are useful and kneading of the muscles to relieve the intolerable cramps. But intravenous saline is the best treatment for this symptom.

Ice and a small hypodermic of morphia may check the vomiting—if, indeed, opium in any form is justifiable in cholera—but it must be remembered when giving drugs subcutaneously in cholera that they remain unabsorbed during the algid stage, and when the reaction sets in the drug or drugs which have been injected may be taken up in quantities which prove poisonous.

Fluid should be given in sips, as large drinks are apt to excite emesis. Stimulants may be necessary. Coramine is useful. Hot red wine, hot tea and black coffee have been recommended.

Native aluminium silicate (kaolin) is claimed to be a specific both for cholera and for acute bacillary dysentery. The method advocated is as follows: To 250 c.cm. of cold boiled water add 100 grammes of kaolin pulverized and shaken until the mixture has become creamy and homogeneous. Give a tumblerful every half-hour, or hour, to six or more doses. Smaller doses are continued over several days. If the patient is too ill to swallow, the mixture should be given by means of a stomach tube.

The standard treatment for cholera, however, is that of Rogers. It is based on the fact that not only is the water content of the blood reduced by an amount varying from one-third to two-thirds, but there is also a loss of saline constituents. Hence the latter must be supplied, and his hypertonic solution for intravenous injection consists of sodium chloride, 120 grains; calcium chloride, 4 grains; sterilized water, 1 pint. This is introduced by means of a special apparatus at the rate of not more than 4 ounces a minute.

Where there is a doubt as to the necessity for the employment of his method, Rogers estimates the specific gravity of the blood. As full particulars are given in the booklet accompanying the cholera equipment nothing further need be said regarding the method here. It seems, however, convenient to tabulate his latest summary of the procedure he now follows :—

1. On admission 1/100th grain atropine sulphate and repeat night and morning.
2. Take specific gravity of blood, blood pressure and oral and rectal temperatures.
3. If blood pressure not over 70 mm. or specific gravity is 1,063 or over, inject 3 to 6 pints of fluid according as specific gravity is 1,063-4-5-6 in adult males. Less for females and children.

   The first pint consists of the alkaline solution mentioned in para. 8, the remainder is hypertonic saline; thus, if 4 pints are indicated, give 1 of the alkaline solution and 3 of the hypertonic, continued through the same flask and cannula.
4. Unless rectal temperature is below 99° F. saline should never be injected at above 98° F. Risk of hyperpyrexia.
5. If rectal temperature is 100° F. or over, give hypertonic solution at temperature between 80° and 90° F.
6. Normal saline, *i.e.* 90 grains NaCl, 1 pint every two hours by rectum till collapse stage past and urination re-established. Then every four hours until 2 pints urine in twenty-four hours.

   If the urine is acid give the alkaline solution mentioned in para. 8 instead of normal saline.
7. Fall of blood pressure to 70 mm. and under, or rise of specific gravity to 1,063 or above, are indications to repeat injections morning and evening and at any time when pulse fails or patient restless.
8. At each intravenous injection, give 1 pint of sodium chloride 90 grains and sodium bicarbonate 160 grains (2 per cent.). (*See* para. 3.)

   N.B.—Sterilize the sodium bicarbonate in paper in autoclave and add to sterile salt solution.
9. Repeat alkaline injection later if urine deficient and blood pressure 100 mm. or more and specific gravity below 1.063. (Normal for Europeans=1,058; for Indians=1,056.)
10. If blood pressure remains persistently much below 100 mm. and urine is deficient, give pituitary extract and caffeine sodium salicylate (5 grains by mouth every four hours). Cup and foment over kidneys.

Where possible a special tin-floored transfusion room should be provided in close proximity to the cholera ward.

In the new Cholera Unit, adapted for the treatment of 100 cases, the principles advocated by Sir Leonard Rogers are closely followed, with some minor modifications. No provision is made for the estimation of the specific gravity of the blood ; instead, reliance is placed on blood pressure estimations and five modern mercurial sphygmomanometers are provided for this purpose in each unit.

It should be here noted that whilst there is no question as to the urgent necessity of fluid, introduced by the quickest possible route, in cholera, it is questionable if hypertonic saline and alkali solutions have any marked advantage over normal saline solution which is simpler to make up and can often be prepared and administered more rapidly than the above-mentioned more complicated solutions. In most cases the general appearance of the patient with his very evident intense dehydration is sufficient indication for an immediate intravenous saline injection, and 4–6 pints may be given immediately in such cases without wasting time in estimating the blood pressure, etc. The general guiding principle should be that if time permits the rigid technique advocated by Rogers (with certain modifications mentioned in the pamphlet accompanying the cholera unit) should be followed. In very urgent cases or where facilities do not exist for the full technique, the simplified technique outlined above may be used.

If rigor follows transfusion use hot bottles temporarily till it is over. Collapsed cases after the rigor may benefit from ¼ grain each of morphia and belladonna extract, but, as stated, opium must always be used with care in cholera.

The other part of Rogers' treatment consists in the administration of calcium permanganate water from 1 to 6 grains to a pint, and 2-grain coated potassium permanganate pills given very frequently at first. Details will be found in the equipment booklet. Continue the pills until the stools become green and less copious. Along with the permanganate 10 minims of a 1/1,000 solution of adrenaline chloride may be given every three hours to re-establish the urinary secretion. Keep the patient warm and apply turpentine stupes to the abdomen. Serum therapy in cholera is still on its trial but promises well. The dose is 40–100 c.cm. intravenously.

The administration of solutions of glucose has been strongly advocated, either a 10 per cent. solution intravenously or an isotonic solution (4½ per cent.) subcutaneously. In view of the results obtained in pneumonia it may be advisable to employ hypertonic glucose (25 per cent.) intravenously. Distilled water should be employed as the solvent, not normal saline.

Lately an old-time remedy for cholera has been revived, with encouraging results. This is a mixture of essential oils given in the following formula :—

Spt. aether.	min. 30
Ol. cajuput.	
Ol. cloves	
Ol. juniper	aa min. 5
Ac. sulph. arom.	min. 15

Dose.—One drachm, in half an ounce of water, every half-hour

until vomiting and purging cease. The same dose is administered to contacts once or twice daily for one or two days.

A useful mixture for the reaction stage is as follows :—

Bismuth. salicylat.	gr. 15
Sod. bicarb.	gr. 5
Liq. opii sedativ.	min. 5
Mucilaginis	q.s.
Aq. chloroformi ad ...	1 oz.

At this stage, also, if the diarrhœa is troublesome rectal injections of tannin, 1 ounce, gum arabic, 1 ounce, and warm water, 1 quart, are indicated.

Inquire as to retention of urine and treat anuria by poulticing or dry cupping over the kidneys.

At a later period alkalies and digitalis will be found useful. A serious symptom to be promptly combated is the occurrence of coma. As there is marked acidosis in cholera, the method of giving 3 per cent. sodium bicarbonate solution by subcutaneous injection seems reasonable. It may be given frequently in quantities up to one litre, if not already employed during transfusion.

The diet for convalescent patients must be very bland and easily digested and the return to ordinary diet carefully regulated.

Much work has been done on both the prophylaxis and treatment of cholera with bacteriophage. The results are, up to the present, inconclusive.

CYSTICERCOSIS*

Cysticercosis is the term given to the somatic infestation of man by cysticercus cellulosæ, the larval or bladder-worm stage of the tape-worm, *Tænia solium*.

There is no authentic record of the infestation of man by cysticercus bovis, the corresponding stage of *T. saginata*, the common tape-worm of this country.

The adult tape-worm, *T. solium*, is a parasite of man alone and normally the larval stage is passed in swine, the parasitized flesh being known as " measly pork."

Formerly cysticercosis was common in Europe, more especially in Germany where uncooked ham was popular. Of late years the disease has become a rarity in this country and practitioners have tended to forget its potentialities ; and it is only comparatively recently that cysticercosis has been recognized as a common cause of a form of epilepsy developing *de novo* in British soldiers returning from service in the East, especially from India.

Etiology.—Since each gravid segment of *T. solium* contains some 40,000 eggs, man, the sole host of the adult worm, may pass from his intestine many hundreds of thousands of eggs at one time. He may under faulty hygienic conditions become the host of the larval

---

* Abridged from the chapter by MacArthur on Cysticercosis in the " British Encyclopedia of Medical Practice," Vol. 3.

cysticercus by the ingestion of tape-worm eggs in uncooked food of many kinds, including water, uncooked vegetables, etc., contamination of which may be direct or through the agency of flies. The human host of the adult worm may contaminate his hands and thence his food with eggs passed by himself and thus suffer auto-infestation and, it has been suggested, another form of auto-infestation may occur by the regurgitation of gravid segments from the gut into the stomach. By whatever path the eggs are introduced into the alimentary tract of man their subsequent development resembles that which takes place in their normal host, the pig. The liberated embryos with the aid of their tiny hooklets penetrate the intestinal mucosa and are borne by the blood stream to their final habitat which, in man, is usually the brain and voluntary muscles. Any tissue or organ may, however, be affected. As regards the brain, the grey matter is invaded more commonly than the white. The parasite may also invade the eye and may occasionally be seen moving in the anterior or posterior chamber of that organ.

The total infestation may vary within the widest limits, from one single cysticercus to many hundreds; infestation may be limited to one organ such as the brain, or be generalized throughout the body.

The morphological development of the cysticercus is completed within three or four months of entry. Except in the brain the cysticerci become walled off by a clear-cut fibrous capsule, the host capsule, the effect of which is to protect both the parasite and the host. In the brain encapsulation to a lesser degree results from the proliferation of surrounding neuroglial tissue together with cellular reaction (Plate 9). In most cases, as long as the parasite remains *alive*, a relative equilibrium appears to be attained between the encapsuled living cysticercus and the host tissues, both continuing to live in a state of symbiosis. When, however, the cysticercus, dies, it acts as an irritant foreign body, liberates toxic products while undergoing degeneration, and exerts increasing pressure on the surrounding tissues through the progressive distension of the cyst capsule by fluid. A further cellular reaction is now provoked and damage to the cyst wall allows widespread penetration of the toxic products of disintegration.

This brief description of the morphology of the cysticercus especially when it infests the brain, may help to explain some at least of the puzzling neurological symptoms connected with its presence in this organ, and why it is that parasites may be lodged in the brain for a term of years (at least six) before they begin to give rise to symptoms; and why these symptoms, when present, may wax and wane in intensity and alter both in character and localization, sometimes in a most dramatic and kaleidoscopic manner.

The duration of life of individual cysticerci varies within wide limits; as a rule they die off gradually so that dead calcified cysts and living parasites may co-exist in the same individual and even the same organ. Many parasites die off between the third and sixth years, though viability for a much longer period is possible. The deposition of sufficient lime salts to cause a shadow in a radio-

graph takes at least three years from the time of death of the parasite, and those cysts which parasitize the brain show relatively much less tendency to calcify than those occurring elsewhere.

Symptoms.—In some cases, infestation of the brain with cysticerci is so overwhelming that the host is unable to withstand the onslaught and dies during the early stage of infestation and development of the larval cysticerci. In these fulminating cases death may result within a week of the onset of symptoms, the clinical picture resembling that of an acute encephalitis; or the patient may develop signs of increasing intra-cranial pressure, leading to coma and death within a few months. In attacks such as these, which are exceptional and consequent on overwhelming infestation, the most characteristic signs of cysticercosis, palpable subcuticular cysts and major epileptiform attacks, may not occur, since they have not had time to develop.

Normally, three clinical stages, with a certain degree of overlap between them, may be recognized. These are :—

(1) The incubation period.

(2) Period of premonitory symptoms.

(3) The established disease.

Incubation Period.—This is the interval between the original infestation and the onset of symptoms. It is usually difficult, for obvious reasons, to establish even approximately when the original infestation took place. Even if the patient was known to have been harbouring an adult tape-worm and therefore passing gravid segments containing eggs from any one of which he might have suffered auto-infestation, he might equally well have been infested by eggs passed by some other carrier. It should be noted that an individual rarely shows signs of the established disease within two years of proceeding to an endemic area.

Premonitory Symptoms.—These occur during the active life and development of the parasite. The symptoms occurring at this stage may be so mild and transient as only to be recognizable in retrospect when the established disease has become manifest. Headache, irregular fever, myalgic pains, often accompanied by transient eosinophilia, may all occur during this phase. In many cases there is a complete absence of such premonitory symptoms, the first evidence of the disease being an epileptic fit or the finding of palpable subcuticular cysts.

Established Disease.—The most objective symptom of this, the final stage, is the finding of one or more palpable subcuticular cysts. The number and positions of these cysts vary greatly from patient to patient and from time to time in the same patient. Cysts, which have been in evidence maybe for years in one site, may collapse and disappear within a few days, whilst other cysts may become palpable in sites where previously they could not be detected. This late appearance of cysts, in some cases spread over a dozen or more years, occurs through the distension of the cyst capsule with fluid, this being associated with the death of the contained parasite. The appearance and disappearance of these

palpable swellings may lead the patient to imagine that his "little lumps" have the power to migrate from place to place.

These little palpable cysts, which are usually about the size of a small pea or bean, but occasionally as large as a pigeon's egg, may be found in the subcutaneous tissue or muscles of any part of the body, head and face, including the eyelids, lips, tongue, trunk and limbs; but they are rarely palpable in the hands and feet although shown to be there by X-ray; if of sufficient size and prominence they can often be seen as well as felt, more easily in some sites (*e.g.* forehead) than in others. They are more commonly found in the upper half of the body than the lower owing to the smaller muscular development and less cover for the cysts in the former. The size and shape of the individual cysts vary with their age and site. In the brain, where they meet an equal resistance on all sides, they tend to be globular and average about a centimetre in diameter; those lying between muscle fibres and separating them are oat-shaped and may attain a length of two centimetres when fully grown. The subcuticular cysts are usually symptomless and one has to look and feel for them as they are seldom complained of. Palpable cysts are not a necessary feature of cysticercosis and the brain may be studded with cysts without any being found elsewhere.

Epileptic attacks constitute the most important presenting symptom of brain infestation and usually develop only when the cysticerci have been present for several years. The epileptic seizures may vary greatly in character. In some they resemble major epileptic attacks so closely that patients have been kept under treatment for so-called idiopathic epilepsy for many years before the true etiology of the condition has been recognized. Other attacks may resemble petit mal; or the patient may have a series of Jacksonian attacks, a feature of which may be that each attack starts in a different group of muscles. The fully developed epileptic seizures or Jacksonian attacks may be preceded for months or years by "larval" attacks consisting of localized muscular spasms which may possibly have been regarded as a hysterical manifestation. The onset of the first epileptic attack may coincide with the appearance of the first subcuticular cyst, or cysts may have made their appearance for a long time—up to six years—before the first fit is registered; on the other hand, the brain symptoms may precede the advent of palpable cysts by months or years. Epilepsy is by no means the only evidence of cerebral involvement and a wide range of symptoms may occur referable to the area or areas of brain attacked. Syndromes closely resembling hysteria, insular sclerosis, neurasthenia, and various psychoses, may occur with or without epileptiform seizures. Indefinite temperamental changes similar to those following epidemic encephalitis may also occur. Whatever form the brain symptoms may take epileptiform seizures or Jacksonian attacks are usually met with at some stage of the disease.

Prognosis.—Prognosis is difficult and must be extremely guarded. The tendency of the disease is steady retrogression to a fatal termination, the fatal issue being preceded by a variety of clinical syndromes mimicking many disease processes; amongst

these may be mentioned status epilepticus, progressive dementia and asthenia, maniacal outbursts which may necessitate residence in a mental hospital, symptoms paralytic or otherwise suggestive of an advancing cerebral tumour or of increasing intracranial pressure, etc., etc. Others progress steadily to a certain stage of chronic invalidism at which they may remain with little further change for better or for worse for many years. The most dangerous period lies between the sixth and the eighth years after the onset of symptoms. Some few cases make an apparently complete recovery after a long series of fits, lasting, maybe, many years.

Diagnosis.—One of the most important factors in the diagnosis of cysticercosis is the " awareness " of the possibility of its occurrence, especially in those individuals who suddenly develop epileptic seizures during healthy adolescent or adult life, particularly if they have served in India or in other stations where infestations with *Tænia solium* are common. This diagnosis is all the more likely to be correct if there is no previous personal or family neuropathic history.

It must be remembered that cerebral cysticercosis may simulate very closely both idiopathic epilepsy and cerebral tumour and in the absence of palpable cysts or of radiological evidence it may be impossible to distinguish them.

The positive diagnosis of cysticercosis depends on one or both of two objective findings. These are :—

(1) The presence of palpable cysts.
(2) Calcification of cysts containing dead parasites.

It must be emphasized that unless the cysts are very superficial they are not palpable before the death of the parasite, palpable cysts being therefore in most cases a relatively late manifestation. Calcification of the cyst is a still later phenomenon and usually at least three years elapse after the death of the parasite before sufficient calcium has been deposited to be seen in a radiograph ; and, as mentioned previously, calcification of intra-cerebral cysts is relatively rare at any stage.

The patient under suspicion should be carefully examined for palpable cysts from top to toe, the muscles being rolled and kneaded under the hands whilst alternately contracted and relaxed. He should be carefully questioned as to whether he has noticed any small lumps at any time and should be warned to look out for their future appearance.

To demonstrate the parasite a suitable cyst is excised under local anæsthesia and examined under the microscope. The hooklets on the scolex are diagnostic and characteristic.

The radiological examination of the patient for calcified cysts is also very important and an exact technique must be carefully followed. The following regions are radiographed :—skull, lateral view only ; root of neck ; upper arms ; fore-arms ; thighs ; legs. The films and intensifying screens should be free from blemish, and note should be made of any blemish on the patient's skin such as tattoo marks. The exposure aimed at should be suitable for bone detail with a slight under-exposure. Exposures suitable to demonstrate soft structures may mislead. Shadows vary from

a small and easily missed " dot " less than a millimetre in diameter, signifying a calcified scolex, to a fully grown elliptical cyst more than two centimetres long. The search throughout the soft tissues must be very thorough. If no calcified cysts can be seen after a thorough search another series should be taken and examined in a year's time, and so on, year after year, as long as the diagnosis remains still in doubt. It must be emphasized that calcified cysts in the brain are rare and must never be expected, although, of course, they must be looked for. (Plates 10–12.)

The calcified cysticerci can hardly be confused with the calcified encysted larvæ of *Trichinella spiralis*, which also parasitize human muscle. The latter are minute and can hardly be seen without a magnifying glass.

A blood count gives little assistance in diagnosis. An eosinophilia may be present during the invasion stage and later when the cysts are degenerating. The cerebro-spinal fluid is but little affected though there may be considerable increase of pressure with a moderate lymphocytosis.

Complement fixation tests, using an alcoholic extract of *Tænia* species as antigen, have proved useful in some cases, although on the whole disappointing.

Cases suspected of suffering from cysticercosis should be kept under observation and thoroughly investigated at regular intervals, a series of radiographs being taken at intervals of one to two years.

Treatment.—Treatment is unfortunately, at the best, only palliative. Phenobarbitone and the bromides are often useful in controlling the fits. From a consideration of the essential pathology of the disease it can be assumed that any larvicide is contra-indicated unless it can be made effective at a very early stage of the infestation.

Theoretically, at all events, we should rather look for an elixir which would enable the larvæ to continue to live in symbiosis with their host to a mutual old age. Surgery, except as an emergency measure, has little scope in the treatment of cysticercosis and is only justified in those cases in which life or some important function is directly threatened. Relief from such interference is usually only temporary.

DENGUE

Dengue occurs chiefly in the tropics, but also extends into sub-tropical areas and as far beyond this as the vector is found. It is most common along littorals, probably because the mosquito *Aedes* (*Stegomyia*) *ægypti* is usually numerous in sea coast places. The disease tends to cause sharp, explosive epidemics, and many pandemic outbreaks have been recorded, these often occurring at about 20-year intervals.

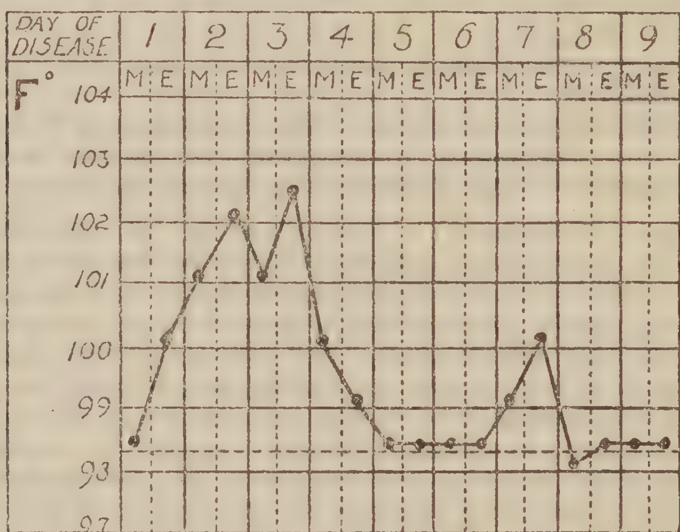
Etiology.—The established vector of the disease is *Aedes ægypti*, as proved by experimental research in Australia, where it has been shown that the blood of patients suffering from an attack of dengue can reproduce the disease when inoculated subcutaneously into

healthy persons, and that infected *Aedes ægypti* transported to a dengue-free locality can cause the disease by their bites. It is due to a virus which is present on the second and third day in the patient's blood, and, possibly, it may persist for a longer period.

Other probable carriers are *Aedes albopictus* and *Armigeres obturbans ;* the evidence regarding *Culex fatigans* is conflicting, and all recent work has failed to confirm the earlier opinion regarding the responsibility of this mosquito in the spread of dengue.

Symptoms.—Incubation is five to nine and a half days according to the Australian work, but in all probability it may be shorter or longer. Onset very sudden, with rapid rise of temperature, which may reach 105° F. Within an hour or two, the so-called initial rash appears. It may be only a blotchy congestion of the face, which looks hot and puffy, or there may be a scarlatiniform erythema,

Fig. 29.

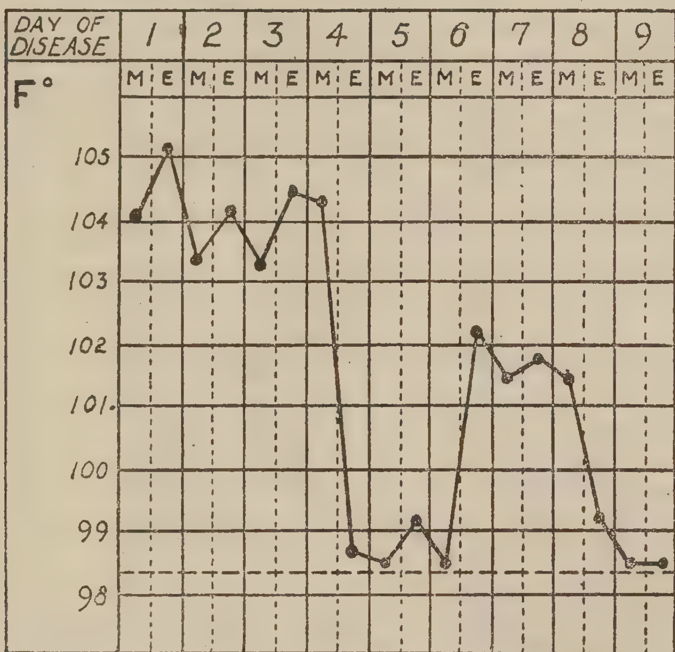


Temperature in mild case of Dengue.

usually confined to the face and extremities. Remember that this primary rash is very transient and is often overlooked. Itching of the palms and soles may occur at the same time. Very soon the patient is suffering from severe headache, chiefly supra- and post-orbital, and the typical joint pains, which are really located in the tendinous insertions about the joints. There is also myalgia, most severe in the back. The condition indeed closely resembles that met with in influenza, but, as a rule, coryzal signs are absent. The ocular muscles are specially affected, and every movement of the eyes causes pain. The pulse is slightly accelerated but soon slows. Swollen glands may make their appearance. Insomnia is present and there is severe mental and physical depression, while malaise and anorexia are marked. A feeling of giddiness is common. Constipation is the rule at the outset. There is no albuminuria. The temperature remains high for three or four days, then drops, it

may be, to normal, continues low for twelve hours to three days, and then rises again sharply (Figs. 29 and 30.) During the interval, which, be it noted, may be absent altogether, the patient feels better, but, with the relapse, the pains and other general symptoms start again. This stage, however, is short, but is marked by the appearance of the terminal rash, and may be signalized by a regular crisis with sweating, diarrhœa or epistaxis. Sometimes a crisis of this kind accompanies the first fall of temperature. The true dengue rash resembles that of measles, begins about the bases of the thumbs and the back of the wrists and soon appears about the big toe and ankle. Then the elbows and knees may be involved, and sometimes the exanthem spreads all over the body. The palms and soles may

Fig. 30.



Typical Dengue.

take on a carmine flush. Desquamation follows when the rash has been pronounced. This second stage may be very brief, or may last for a couple of days.

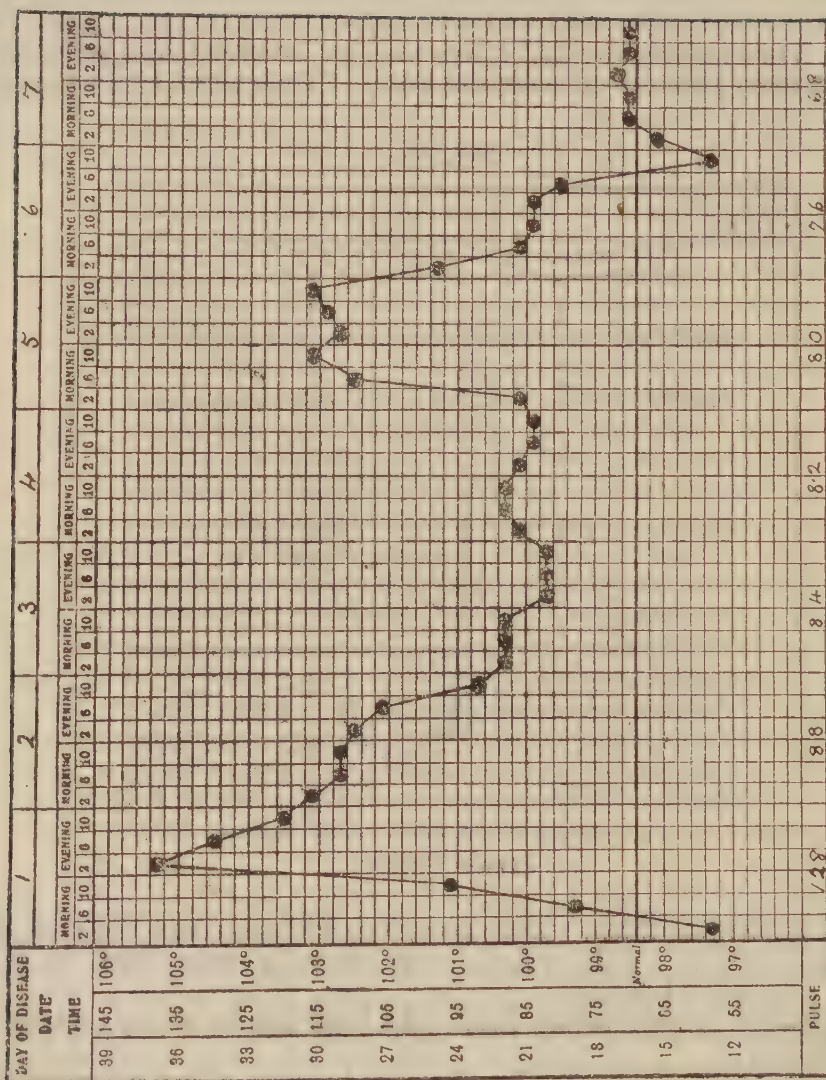
The disease is very rarely fatal, and then nearly always owing to complications.

Convalescence is apt to be slow and marked by neurasthenic symptoms such as mental irritability or depression.

Leucopenia and reduction in the polymorphs constitute the most marked blood changes. There is also an increase of lymphocytes and a late eosinophilia. Eosinophilia is recorded most frequently in localities where helminthic infections are common, and possibly may merely indicate a return of the blood to its pre-febrile condition.

While the above symptoms are those of typical dengue, it must be remembered that there are so-called six and seven-day fevers

Fig. 31

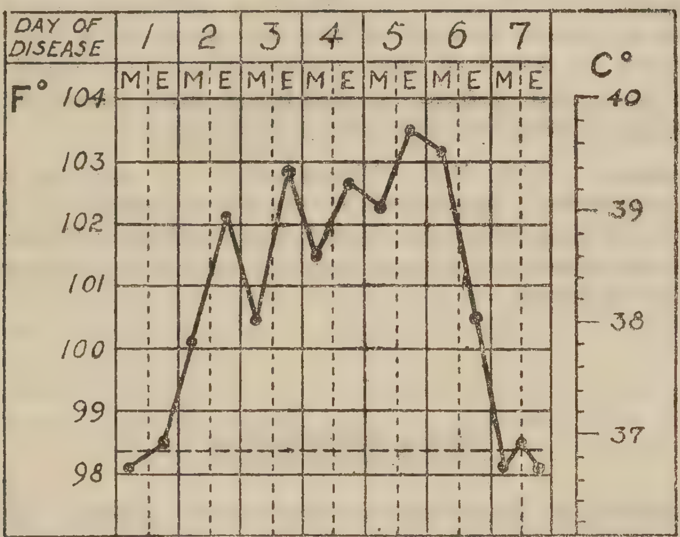


Saddle-back Temperature in case of Seven-day Fever—Typical Dengue.

which, for all practical purposes, may be classed as dengue. In these the typical saddle-back temperature (Fig. 31) may be lacking, the pyrexial record being continuous, the spleen may be slightly enlarged, and one or both rashes may be absent. Researches in the Philippines show that dengue may be so mild in its manifestations as to be unrecognizable with certainty except by transmission experiments, and that an infected person may even remain afebrile throughout and yet be capable of infecting mosquitoes. Immunity after attack is very variable in degree.

Differential Diagnosis.—It must be differentiated especially from influenza, yellow fever and phlebotomus (sandfly) fever, and to a less extent from malaria, early enteric or paratyphoid, scarlatina, measles, early small-pox and rheumatism. Mild infections due to *Leptospira icterohæmorrhagiæ*, and to allied species or strains, may

Fig. 32.



Atypical Dengue simulating Early Typhoid or Paratyphoid.

have a close resemblance to dengue, but differ in that albuminuria seems to be a constant feature. Rift Valley fever, first described in Kenya Colony in 1931, resembles dengue in many respects. This disease, which occurs from time to time as a fatal epizootic amongst ewes and lambs, also attacks those in close contact with them, such as shepherds, also laboratory workers. The causal organism is a virus and is supposed to be transmitted by a mosquito, *Tæniorhynchus brevipalpis*.

The almost invariable respiratory involvement in influenza is a distinguishing character, while the rash of dengue is absent in influenza.

In yellow fever albumin will be found in the urine at an early date.

Blood inoculation intracerebrally into mice causes no symptoms, thus differentiating dengue from yellow fever and Rift Valley fever.

Although typical dengue is easily distinguishable from typical sandfly fever on account of the longer course, relative severity, and

secondary rash, usually met with in the former, atypical attacks of either may be impossible to differentiate on clinical grounds alone.

Indeed, some declare the two diseases to be identical, and we are led to ask if the same disease in altered form may not be transmitted by totally different insect vectors.

For the present it is clearly advisable to consider dengue and phlebotomus fevers as separate and distinct diseases and to allot a section of these Memoranda to each of them ; admitting, however, that, in many cases, the short form of dengue is clinically indistinguishable from sandfly fever.

The onset of dengue is different from that of malaria, but may resemble the early stage of typhoid and paratyphoid (*see* Fig. 32). Careful observation should, however, serve to distinguish dengue from these fevers and from the other diseases mentioned above.

Prophylaxis.—Destroy domestic mosquito-breeding places and protect from mosquito bites by repellants, such as one part of oil of bergamot in 16 parts of kerosene, citronella oil in vaseline, 50 per cent. alcoholic solution of thymol or oil of cloves in lanoline and glycerine, or some of the preparations mentioned on p. 36. Where possible, nets should be employed and, under certain conditions, trapping may be used with advantage.

Treatment.—Light diet. Phenacetin and aspirin relieve the pain and headache. Morphine is rarely necessary and is better avoided. Cold spongings are useful, especially for the insomnia.

During convalescence, where there is much depression, a sound wine may be ordered.

DIARRHŒA

Acute diarrhœa unconnected with any specific infection or disease is often encountered in the East. Common causes are, exposure to chill, and irritation of the bowel by sand and dust or by coarse and unsuitable food. Diarrhœa due to the last-named cause was prevalent amongst African troops and followers during the war of 1914–18, and in East Africa water containing large quantities of decaying vegetable matter appeared to be the responsible agent.

All cases of acute diarrhœa, however, must be regarded with suspicion, and the possibility of dysentery, bacterial food-poisoning and cholera carefully excluded by the appropriate examinations.

Treatment.—In acute diarrhœa the early administration of astringents is unwise, and especially so if the nature of the attack is in doubt. If the patient is not already faint and weak, give an ounce of castor oil, preferably in brandy, pouring the oil carefully into the centre of an ounce of brandy, and then adding an ounce of water. Failing the brandy, black coffee helps to mask the taste and " feel " of the oil. Some prefer to administer the castor oil throughout the period of starvation (*see* below) in teaspoonful doses,

made up as an emulsion, every four hours. Instead of castor oil, calomel (gr. 3 with gr. 15 of sodium bicarbonate), or magnesium sulphate ($\frac{1}{2}$ oz.) may be employed.

Whatever evacuant is used, starve the patient after administration for from twelve to twenty-four hours, during which time he should be encouraged to take fluids, such as water or hot tea, freely. Complete rest in bed is highly desirable. After the purgative has acted sufficiently, if one is satisfied as to the simple nature of the diarrhœa, commence to give bismuth carbonate gr. 15 and salol gr. 5 in one powder, the dose being repeated every two hours for about ten doses. If desired, larger quantities may be given over a shorter period. Or a mixture like the following, taken four-hourly, may check the diarrhœa satisfactorily :—

Tinct. opii	min. 10
Spt. ammon. arom.	min. 30
Ess. menth. pip.	min. 20
Tinct. catechu	1 drachm
Aqu. ad	1 oz.

For distension and colic nothing is better than two teaspoonfuls of paregoric in hot water, repeated every two hours for two or three doses.

When catharsis is exhausting, or griping very severe, a hypodermic injection of morphia and atropine may be given, but is better avoided unless necessary. Remember that cholera may commence, especially in Europeans, with a preliminary stage of diarrhœa, and that in this disease opium is hurtful, except, according to some authorities, at the outset.

Apply heat to the abdomen. A hot bath, when it can be managed, sometimes acts like a charm, and in diarrhœa due to chill and exposure even bathing the feet and legs in hot water and mustard does good.

After the period of starvation has been completed, give hot milk diluted at first (one part to four parts of rice-water), Benger's food, or gruel of any kind, and gradually work up to a normal diet.

Acute Gastro-Enteritis in Children

This is often a manifestation of infection with one or other of the dysentery bacilli. Whatever the cause may prove to be, do not wait for a laboratory diagnosis but commence treatment without delay. Remember that malaria may be a cause of diarrhœa in children.

The following, in the main, is the treatment advocated by Green-Armytage.

Indications.—(1) Get rid of the poison, and so allow the inflamed intestine to recover. (2) Counteract acidosis. (3) Supply the fluid lost—dehydration is the common cause of death. (4) Provide a proper diet.

These indications, in the sequence given, may be met as under :—

(1) Half-hourly, or hourly, doses of

Sod. sulph.	gr. 20
Sod. bicarb.	gr. 10
Sod. cit.	gr. 10
Glycerin.	min. 20
Aq. anisi	1 drachm

until stools become watery and brown.

If there is vomiting, wash out the stomach with 1 per cent. sod. bicarb. given through a catheter and funnel. If the vomiting is very severe, give gr. $\frac{1}{10}$ of calomel every hour for six or eight doses. One-minim doses of tinct. chlorof. et morph. co. are often useful.

(2) Half-a-teaspoonful of sod. bicarb. and half-a-teaspoonful of common salt to one pint of boiled water, add $\frac{1}{2}$ gr. of saccharine to make palatable. The child is encouraged to take as much of this as possible. The salt makes it thirsty and so it drinks more readily. If œdema is present, give the drink without salt.

Raisin tea.—One tablespoonful of white raisins to one pint of boiling water, crush and strain. Infants and small children readily take one ounce, or more, an hour.

(3) In mild and early cases, the alkaline solution given under (2) suffices. Infants will take two pints in twenty-four hours almost continuously if given through an easy teat.

In late and severe cases, 4–6 ounces of saline given under the skin of the axilla every five hours. If the child is extremely ill, give the saline intraperitoneally—pick up the abdominal wall just below the umbilicus, pass in a large Record-syringe needle at right angles for 1$\frac{1}{2}$ inches, release hold on abdomen, and inject a pint of saline.

(4) Nothing but rice-water prepared as follows :—One tablespoonful of rice to 1$\frac{1}{2}$ pints of water; boil, strain, add a pinch of salt and a teaspoonful of brandy.

After forty-eight hours, give whey, or skimmed milk diluted 1 in 3.

Instead of subcutaneous injections of saline, 5 per cent. glucose may be given combined with injections of insulin.

If there is reason to believe that an attack is of dysenteric origin, serum should be given in a 20 c.cm. dose subcutaneously.

DYSENTERY

Dysentery is a term denoting a symptom complex, namely the passage of blood and mucus from the bowel, and may be due to various pathogenic agents.

From earliest times dysentery has been, beyond others, the disease of armies in the field, and again during the last war it was the most common medical cause of inefficiency. Not only so, but

it was responsible for many deaths, and left many men more or less permanently disabled.

Despite statements to the contrary, it may be confidently asserted that in each of the Eastern war areas the bacillary type was more prevalent than the amœbic. Indeed, it would seem that *epidemic* dysentery, with a few notable exceptions (*e.g.* the recent Chicago epidemic), is always of the bacillary type. The amœbic form, however, was present in all these war areas, more especially in Mesopotamia and East Africa. Indeed, where Indian and native African troops are employed it is probable that much more amœbic dysentery occurs than is the case in areas where only European troops operate. In Macedonia only about 5 per cent. of the dysentery cases were amœbic.

Dysentery due to two intestinal protozoa, the flagellate *Giardia lamblia* (doubtful) and the ciliate, *Balantidium coli*, to the malignant malarial parasite *P. falciparum*, and dysentery caused by the trematode worm *Schistosoma mansoni*, are forms which must not be forgotten. There are also other causes of dysentery, such as ulcerative colitis of unknown origin, but these need not be discussed here.

Much is heard of "flagellate dysentery," but there appears to be no proof that any intestinal flagellate of man is pathogenic. The evidence of possible pathogenicity is strongest as regards *G. lamblia*, but in some instances a low degree of infection with *Entamœba histolytica* is overlooked because of the large numbers of *Giardia* present in the stools. As Dobell forcibly says, "Often we read that some intestinal flagellate was the 'cause' of a patient's intestinal disorder because 'no other cause could be found.' The absurdity of such statements is obvious. If such reasoning were permissible, one would have to suppose that many cases of diarrhœa, in which neither flagellates nor other organisms can be found, are due to no cause at all."

Note.—With a view to prompt and proper treatment, it is of the utmost importance to diagnose the nature of the case as early as possible. Any medical officer not submitting the stools of his dysentery patients for laboratory examination, where facilities for such exist, is guilty of criminal negligence.

AMŒBIC DYSENTERY *

The cause is *Entamœba histolytica*. *E. coli* and the other entamœbæ shown in Fig. 35 and so frequently found in the stools are non-pathogenic. The differences existing between both the vegetative and cystic forms of three of these entamœbæ are also shown in the figure. The important point for the clinician and sanitarian to remember is that the vegetative forms of the dysentery amœba, *i.e.*, those which throw out pseudopodia, absorb nourishment and manufacture toxins, are not resistant outside the body. They easily perish, but this is not true of the cysts, which, so long

---

* *Entamœba histolytica* is responsible for lesions other than dysentery. The lesions due to this organism, wherever they may be, are grouped under the general heading **Amœbiasis.**

as they are in contact with a little moisture, remain alive, and if swallowed are capable of causing infection. These cysts are chiefly found in the solid or semi-solid fæces of the convalescent, and hence the post-dysenteric, whether convalescent or in good health, is the carrier and the principal danger in camp life. Apart from the carrier, infection may take place through the medium of water, uncooked moist food, flies, wind, soiled toilet-paper blown from open latrines, and possibly also from dust, provided the cysts have not had time to dry and perish. It has been definitely shown that house flies, and some other allied species, take up living cysts from infected stools and transmit them in their excreta to food or drink.

When the cysts are swallowed they pass through the stomach and excyst in the intestine. The liberated amœbæ are pathogenic and establish themselves in the large intestine.

The incubation period in amœbic dysentery is variable, often over 60 days, in contrast to bacillary dysentery in which it is usually less than a week.

This form of dysentery occurs as an endemic or sporadic infection, and there is no doubt that our knowledge regarding it and its cause is still defective. For example, it has been shown that a considerable number of apparently healthy people who have never been out of England, where amœbic dysentery is not generally recognized as endemic, may harbour *E. histolytica*. Hence it would seem that it is only under certain conditions, of which we are as yet ignorant, that this protozoon manifests itself as a pathogenic agent.

A recent theory held by some authorities is that those cysts, morphologically typical *Entamœba histolytica* cysts, which may be found in the stools of a proportion of individuals in this and other countries where endemic amœbiasis only occurs as a great rarity, belong to a closely allied but non-pathogenic race.

Symptoms.—Two chief types of amœbic dysentery may be distinguished, one with an insidious onset commencing with diarrhœa and without much general disturbance, the other more acute with severe griping. In the former, three or four pultaceous stools may at first be passed in the day, and there is often tenderness over the cæcum and along the line of the large intestine. Very acute attacks are rare. The onset as a rule is much more gradual than in bacillary dysentery.

Dysentery is more common in the subacute form which, after premonitory diarrhœa, starts with griping pain in the right and left iliac fossæ, often severe, and the frequent passage of motions containing blood and mucus, such passage being associated with much straining and, if the rectum is involved, tenesmus. Usually, when the disease is established, there are about ten to fifteen in the twenty-four hours. At the start they may contain merely dark fluid blood and mucus. The latter is not so sticky, nor is the blood so bright as in bacillary dysentery. The stools have a foul odour. Later, when ulceration has proceeded apace and the blood is decomposing, the appearance of the stools has been aptly likened to anchovy sauce.

Solid stools coated with clotted blood and mucus may be passed at periods when the condition is quiescent.

As a rule there is no fever, but nausea and vomiting often occur, the tongue is moist and coated, and there is anorexia. The disease

tends to recovery, save in the somewhat rare forms with fever and toxæmia, but may pass into a chronic type while hæmorrhage or gangrenous complications may supervene. The hæmorrhage may cause death, the gangrene may result in fatal perforation, or mere exhaustion may kill the patient. Hepatitis and liver abscess are a not infrequent complication and should always be kept in mind.

In chronic cases fever is absent unless there is hepatitis, and the patient presents little sign of illness beyond vague intestinal discomfort, a progressive weakness, the passage of frequent stools, and a steady loss of weight. The skin becomes dry and sallow, and neurasthenic symptoms appear. The stools vary. They may remain merely pultaceous, or become gradually mucoid and show streaks of blood. Mucus alone may be present. Very often this chronic course is punctuated by exacerbations, when there is abdominal pain and some tenesmus. Gangrene may supervene and sloughs be passed.

A latent form of amœbic dysentery requires special mention, for it is apt to escape notice and is probably a fruitful source of "carriers." Further, this class of case when untreated may develop acute attacks or liver abscess. Sometimes a history of occasional diarrhœa, sometimes symptoms suggesting appendicitis, sometimes complaints of indigestion arouse suspicion. Then, where possible, a saline should be given and the stools examined for amœbæ.

Morbid Anatomy.—The ulcerative process, brought about chiefly by the amœbæ burrowing down to the submucosa and elaborating their toxins, is confined to the large intestine; the cæcum, hepatic flexure, and sigmoid being most frequently affected. The appendix and the rectum may be involved, and, occasionally, the lower foot or so of the small intestine. The condition found *post mortem* varies from nodules of infiltration surrounded by a red ring of dilated vessels to large circular or oval ulcers with undermined edges, the latter having the longer diameter, lying as a rule, transversely. They have been described as button-holed or funnel-shaped on section, and have sloughing bases. Stretches of healthy mucous membrane intervene between the affected areas. Ulcers often coalesce, and as a result large tracts of the mucosa may present a worm-eaten aspect. In advanced cases thrombosis of vessels occurs, the ulcers may be covered with necrotic sloughs, and the bowel wall at these places considerably thinned. The gut, on the whole, is much thickened throughout the affected area as a result of exudation and œdema. This specially applies to the region of the cæcum which, on palpation, may closely simulate an appendix abscess, tuberculosis or carcinoma of the colon. These few notes will serve to illustrate points in the pathology and treatment of the disease.

Diagnosis.—Apart from what can be gathered by an inspection of the stools and clinical symptoms, the diagnosis depends on the detection of *E. histolytica* in the motions. Without going into details, it may be said that dysentery amœbæ in warm and undecomposed stools are actively motile and may contain ingested red cells. These qualities serve, in unstained specimens, to distinguish them from the harmless but common *E. coli*, which is not so motile and never contains red blood corpuscles, and from the macrophage cells

commonly seen in bacillary dysentery stools; these may contain red blood cells but are non-motile. Other entamœbæ which somewhat resemble *E. histolytica*, but are non-pathogenic, are shown in Fig. 35. The stools of amœbic dysentery are rich in motile micro-organisms and eosinophiles (Plate 15).

Differential Diagnosis.—From bacillary dysentery by microscopic examination of the stools and bacteriological tests. The mucus of the bacillary dysentery stool practically wholly consists of an exudate made up almost entirely of pus, intestinal epithelial cells, and large macrophages (Plate 16). This is not a feature of the mucus of the amœbic stool. Clinically the diseases can rarely be differentiated, though a severe onset and rise of temperature suggest the bacillary form. The idea that a diagnosis can easily be made from the mere appearance of the stools is entirely fallacious, but it is true that the large number of pus cells in the mucoid stool of bacillary dysentery tends to give it a whitish appearance, while in amœbic cases the colour is brown or greyish green. As stated, the blood in the latter is darker than in bacillary cases. It must be remembered that the excretion of *E. histolytica* is frequently intermittent, hence several examinations of the fæces at appropriate intervals are often necessary.

In doubtful cases an examination with the sigmoidoscope may clear up the diagnosis.

Complications.—Hepatitis, liver abscess, intestinal gangrene, peritonitis and hæmorrhage may be mentioned. The attack may be followed by chronic constipation accompanying a condition known as "dry recto-colitis," in which emetine has been found beneficial.

Cutaneous Amœbiasis.—A rapidly spreading ulcerative process involving the skin may occur :—

(1) About the anus in cases of amœbic colitis or dysentery.
(2) Subsequent to drainage of an amœbic abscess of the liver.
(3) Round a colostomy or appendicostomy wound.
(4) Without any direct visceral connection.
(5) An allergic "amœbic dermatosis" which includes also anal pruritus, urticaria, and acne rosacea.

All these forms of cutaneous amœbiasis usually respond satisfactorily to treatment with emetine.

Prognosis.—Untreated or wrongly treated cases may go from bad to worse, become chronic or lead to liver abscess. The importance of early, correct and efficient treatment cannot be overrated. Carefully wash the stools and examine for sloughs from time to time, as their presence or absence shows how the case is progressing.

It must be remembered that amœbic dysentery is very prone to relapse.

Dietetic Treatment.—Milk can be given almost from the first in most cases of amœbic dysentery, and a low-residue but nourishing diet a few days later.

Give food in small quantities frequently, and see that it is neither too hot nor too cold. Alcohol is hurtful.

Medicinal Treatment.—Begin with an ounce of castor oil, unless the patient is feeble or exhausted, when ½ oz. will be sufficient. In hot countries castor oil sometimes acts as a severe purge, so it is well to be careful in administering it. If colic is present add 10 drops of tinct. opii to the dose. This, with rest, warmth and proper diet may abort an attack of what appears to be commencing dysentery.

The treatment of acute amœbic dysentery falls into two stages. In the first, where active symptoms are present, emetine in some form is necessary. This will check the symptoms and occasionally cure the disease. Unfortunately, as in the case of other protozoal infections, amœbic dysentery is difficult to eradicate and tends to relapse. Therefore on the completion of the selected course of emetine, the assault on the parasites should be continued by administering some of the other medicaments known to be effective. Prolonged or repeated courses of emetine must not be prescribed recklessly, for the drug may cause various unpleasant and serious symptoms, which include depression and debility, cardiac disturbance, and even peripheral neuritis with paralysis affecting the legs and arms. Sometimes emetine has curious effects on the nails, causing ridging and great enlargement of the basal lunule.

Emetine hydrochloride.—Undoubtedly the most effective remedy for controlling the acute symptoms. One grain, dissolved in sterile water, is given hypodermically or intramuscularly every day, either in one dose, or divided into two half-grain doses. The total amount of emetine administered should not exceed 12 grains. The patient should be kept strictly in bed while taking emetine, in view of the possible ill-effects on the heart.

Emetine bismuth iodide.—This compound contains 1 grain of emetine in every 3 grains. The usual course is one dose of 3 grains daily for twelve consecutive days.

E.B.I. should be given in a hard gelatine capsule or pill, for, contrary to what has been stated, the gastric juice may liberate emetine from the compound. It is important to remember that emetine in pill form may be passed unchanged.

Nausea and vomiting must be expected early in the course, but do not diminish efficacy of treatment. Give the dose in the evening along with a cup of hot tea, on an empty stomach, when the patient is in bed. If the vomiting is found to be severe and occurring shortly after the drug is swallowed, administer 10 to 15 minims of tinct. opii before the emetine is given ; keep the patient flat on his back with the head low, and warn him not to swallow his saliva.

Towards the end of the course, E.B.I. may cause a certain amount of diarrhœa, but this rarely requires any treatment.

Emetine periodide.—This is given in 2-grain doses, three times daily, in gelatine capsules, after food. The course lasts for fifteen days, and can be repeated after ten days' interval if required. This compound is less effective than E.B.I., but owing to its more stable composition, the patients escape the nausea, vomiting and depression which frequently attend the use of E.B.I., a very important con-

sideration in dealing with persons who have recently been vigorously treated with emetine.

The following preparations, though less active amœbicidal agents, are beneficial as follow-on treatment after emetine, or they may be given with some form of emetine in a combined course, as mentioned already. They are especially useful for patients who are suffering from the effects of prolonged treatment with one or other of the ipecacuanha derivatives :—

Stovarsol (acetyl-oxy-amino-phenyl-arsenic acid) may be given in 4-grain doses once or twice a day, by mouth, either alone or in conjunction with one of the emetine preparations. A week's course is usually recommended, but this period may be extended up to a month if the patient is deriving benefit, for, unlike emetine, stovarsol is an excellent general tonic. Some persons are intolerant of the drug and may develop an erythematous or papular rash, or even a severe dermatitis.

Carbarsone (4-carbamino-phenyl-arsonic acid) is allied to tryparsamide and stovarsol. The dosage and indications are the same as for stovarsol. The clinical action is due to the content of arsenic and it is said to be less toxic than stovarsol.

Yatren * (iodo-oxyquinolin-sulphonic acid) is best administered by rectal injection, 200 c.cm. of 2 per cent. yatren solution being given after a preliminary washout with 2 per cent. sodium carbonate. It must be retained for several hours.

The best combined treatment is to give sufficient emetine by injection to control the acute symptoms ; then E.B.I. 3 grains by pill or capsule by the mouth daily for twelve days, combined with a yatren enema each day ; and finally stovarsol or carbarsone 0·25 gramme by mouth twice daily for a further twelve days. This course of treatment gives a high proportion of cures.

Kurchi bark.—This extract has a marked anti-dysenteric action, especially in cases of chronic dysentery. It may control the symptoms and keep the patient in good health when other drugs have failed. Up to 2 drachms may be given three times a day and continued for three weeks or longer if necessary. No ill-effects appear to follow its prolonged use.

The seeds of the plant ispaghul (*Plantago ovata*) may be used as a non-specific demulcent in the treatment of the more chronic stages of all forms of dysentery. The seeds, which are procurable in most native bazaars for a few annas, are first of all well washed in several rinses of boiling water and are then left in water over night. They are served in the form of a porridge with milk or water the following morning.

General.—Save in mild cases, it is well to give a saline mixture once a day, *e.g.* ½ ounce of sodium or magnesium sulphate. This prevents constipation, washes away cysts, diminishes the risk from toxins and of septic absorption, and possibly aids the emetine to get at certain of the entamœbæ lying at the base of, or amongst, necrosed

* British equivalents—Chiniofon B.P., Quinoxyl, Quiniosulphan

tissue. It also benefits the colitis, and the same end may be served by the administration of enemata of warm water or saline. A hot bath affords relief, while a soothing injection is made by soaking an ounce of linseed for several hours in 2 pints of warm water.

In all cases the tendency to heart failure must be guarded against. Hypodermics of camphor are indicated (2 grains in 10 minims of olive oil).

Avoid opium unless the colic is severe or the tenesmus distressing. In the latter case employ it with bismuth and thin starch as an enema, bismuth 2 drachms, tincture of opium 30 minims and starch mucilage 2 ounces. A tight flannel binder sometimes eases the pain of straining.

During convalescence, if diarrhœa persists, salicylate of bismuth is very useful. In some cases carbonate of bismuth in large (1 oz.) doses throughout the attack has been found to do good.

As regards complications, liver abscess should not occur in properly treated cases, but if it shows signs of developing, emetine will usually cut it short and cause a cure. (*See* Hepatic Abscess.)

Turpentine stupes to the abdomen are useful in severe colic. Hæmorrhage is to be met by morphia, chloride of calcium, or blood transfusion.

The tendency to collapse induced by the draining of the patient's fluids and the action of toxins is best met by giving intravenous saline infusions as in cholera, but these must be administered in time. It is no use waiting till the patient develops a Hippocratic countenance. A timely infusion may ward off this sign of impending death.

Prophylaxis.—Careful disinfection of stools is essential and the cyst-carrying convalescent should be kept in mind. It is of special importance to see that company cooks are not suffering from diarrhœa or dysenteric symptoms, and no one who has suffered from dysentery should be employed in the handling of food until freedom from infection has been established by laboratory examinations.

The sanitary arrangements for post-dysenterics require special care. They must thoroughly wash and scrub their hands after going to stool, and every effort must be made, as by the provision of fly-proof and wind-proof box latrines, etc., to prevent them infecting others.

Yorke found the following solutions lethal for cysts both at 37° C. and at ordinary temperatures: $HgCl_2$, 1 : 2,500; formaldehyde, 0·5 per cent.; carbolic acid, and lysol, 1 per cent. Chlorine as used for the purification of water had no effect. Cysts kept in fæces at ordinary temperatures died within ten days, and in water within three weeks.

BACILLARY DYSENTERY

The cause is usually either Shiga's bacillus or bacilli of the Flexner or Sonne type. Others may be operative, but do not require mention here. Shiga infections are the most serious because of the potent exotoxin formed. Rarely *B. dysenteriæ* may be found in the peripheral blood.

Like typhoid, the spread of bacillary dysentery may be said to be due to careless carriers, contact cases, chiefly cooks, dirty drinking

water, the dust of dried dejecta and the repulsive regurgitation, dangerous droppings and filthy feet of fæcal-feeding flies fouling food. In this connexion it may be noted that dysentery bacilli have been recovered from flies two or three days after their absorption by these insects.

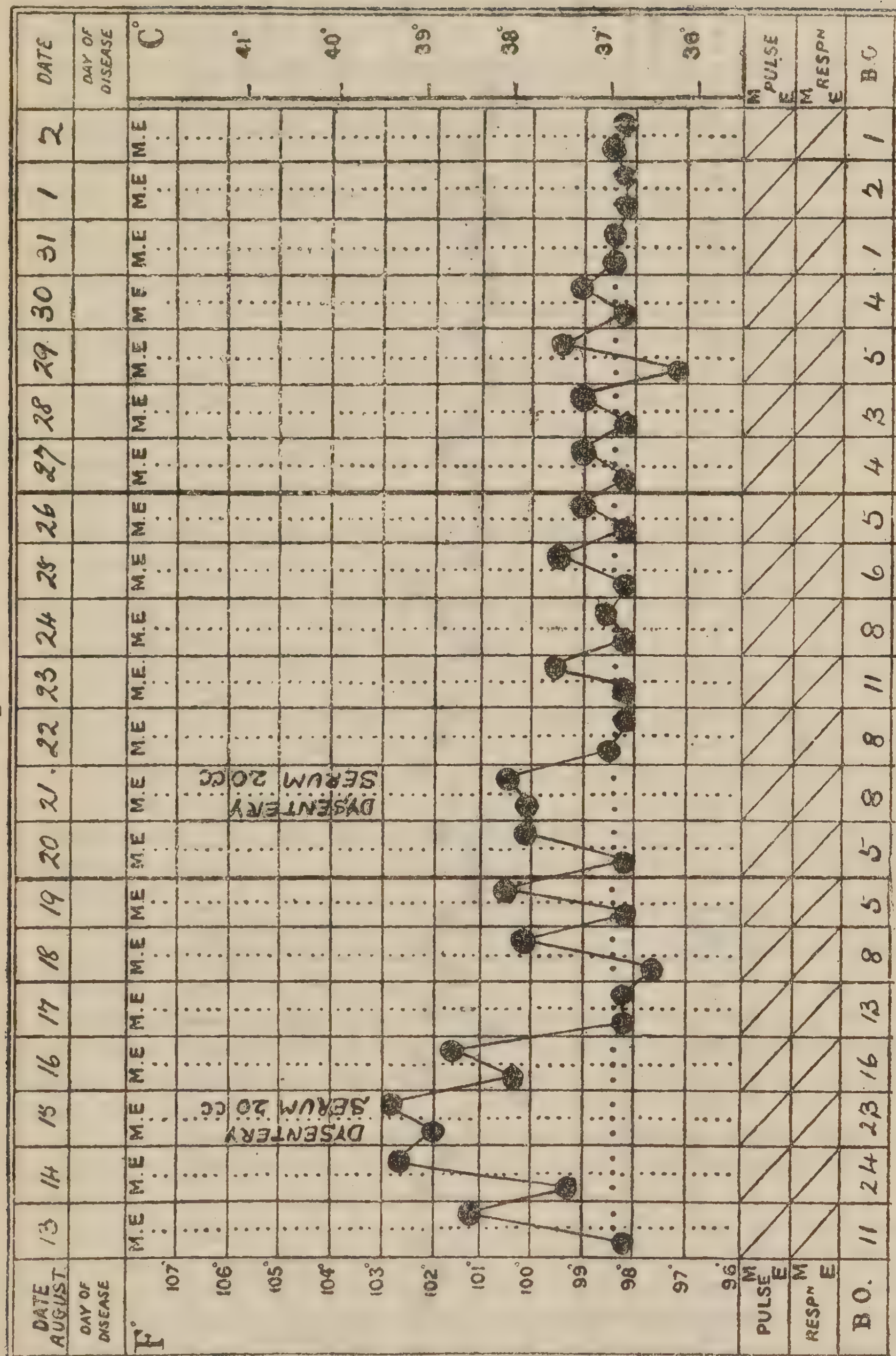
Symptoms.—The incubation period would appear to vary from twenty-four hours to seven days. The symptoms vary greatly according to the severity of the attack. In the very mild cases the illness may be confined to the passage of loose motions, containing little or no blood or slime, associated with only slight fever. In the more severe cases, however, the onset, which may follow a premonitary diarrhœa or constipation, is sudden and attended by pain and an urgent call to stool. At first the motions are normal, but as the attack advances the colic grows more severe, straining and tenesmus set in, there is diarrhœa, and soon the fæculent matter is mixed with bright red blood and mucus, while later the blood and mucus predominate and finally constitute the whole motion. There is great discomfort about the anus, which becomes inflamed, excoriated and very painful, and the bowel may prolapse. Vesical tenesmus may occur and the urine is diminished in quantity. The tongue is moist and coated with a white fur, nausea is frequent, vomiting comparatively rare. The temperature usually rises somewhat and may be considerably elevated, a contrast to what occurs in the amœbic form (Figs. 33 and 34). The number of stools is generally from fifteen to thirty in the twenty-four hours, but it may become excessive and exceedingly exhausting to the patient. The thickened bowel may be capable of palpation if the abdomen is not too tender. As already stated, the stools, being markedly muco-purulent, are often white like milk, but they are rarely free from blood, which usually occurs as flecks or streaks.

When the small intestine becomes involved, for this sometimes occurs and is very dangerous, the temperature remains elevated and general symptoms are much more severe, though the tenesmus is less and the stools fewer. In ordinary ulcerative cases the prognosis depends on the quality rather than on the quantity of the stool. The patient is often heavy and drowsy and exhibits rather a characteristic bluish-red flush on the cheeks. Such cases are usually Shiga infections. It is well to remember that the small intestine, if not involved, may be full of fæcal matter, *i.e.* there may be a local spasm accompanying the diarrhœa and causing distension.

There is a serious type of case in which the muco-purulent stool becomes serous and the patient rapidly wastes. It is this type which is specially prone to cholera-like collapse. In any of the forms gangrene may ensue and offensive sloughs be passed. Toxæmia is then usually very marked, the tongue becoming dry and glazed, the pulse thready and a low muttering delirium supervening. Hiccup may set in and prove exhausting.

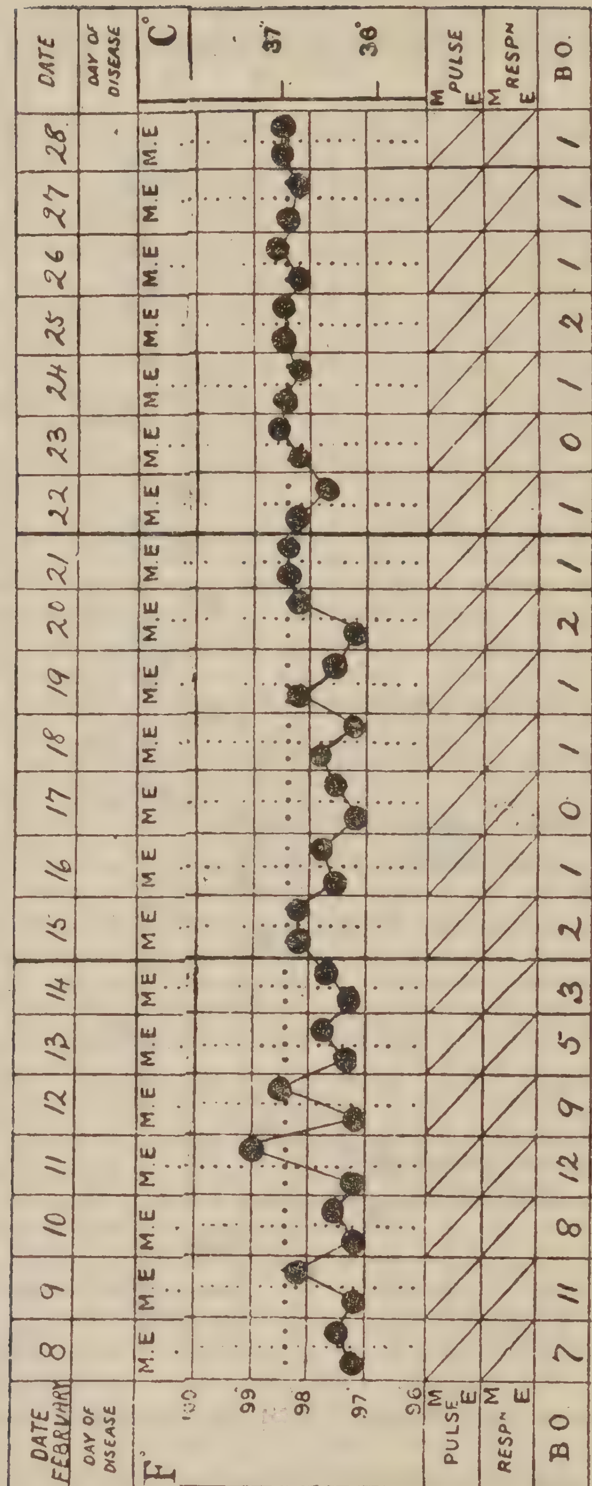
It will be seen that bacillary dysentery tends to be more acute and more toxæmic than the amœbic type. Cases may be classified on a clinical basis, as: 1. Mild (patient apparently well but passing a little blood and mucus). 2. Catarrhal. 3. Ordinary ulcerative. 4. Fulminating. 5. Choleraic (Fisher). In toxæmic cases the diarrhœa is of secondary importance to the toxæmia.

Fig. 33.



Bacillary Dysentery.

Fig. 34.



Amœbic Dysentery

A chronic form, however, is also known, that is to say, a form more or less chronic from the outset, characterized by frequent stools containing blood and mucus, digestive troubles and progressive weakness, anæmia and neurasthenia.

Morbid Anatomy.—In the earlier stages the appearance of the mucous membrane of the large intestine has been aptly compared to lustreless red velvet. This is due to an acute inflammation which may also involve the lower third of the ileum, although Peyer's patches remain unaffected. Later there are areas of blood extravasation beneath the surface and irregular islands of greyish membrane surrounded by hyperæmic and swollen gut. The condition is one of diffuse superficial coagulation necrosis, and the small ulcers are not deep as in the amœbic form. When necrosis is advanced nothing is left of the mucous membrane but a dark green or blackish substance which contains no vestige of gland tissue. This stage of absence of secreting glands is shown clinically by the absence of mucus in the rectal discharges which now have the appearance of "meat washings".

The other viscera exhibit signs of the acute toxæmia which is such a feature of the condition.

Diagnosis.—Macroscopically the stools consist solely of blood and tenacious mucus, red streaks or specks in a whitish medium, and adhere to the bottom of the receptacle. The blood is bright red, the stool odourless, an important point. Later the mucus assumes a yellow tinge and bile or liquid grey fæces may be present. In bad cases offensive green necrotic sloughs may appear and at this stage the stool may resemble that of amœbic dysentery.

Microscopically many undamaged pus cells and red cells are seen, together with large refractile macrophage cells derived from the submucosa and often containing red blood corpuscles and polymorphs. These cells have again and again been mistaken for dysentery amœbæ. There is an absence of motile micro-organisms (Plate 16).

The bacteriological diagnosis cannot be here considered.

Sigmoidoscopy should never be forgotten if the diagnosis remains in doubt.

Differential Diagnosis.—That from amœbic dysentery has been mentioned. Schistosome dysentery must be borne in mind, and in the more chronic cases the possibility of tubercle, cancer and syphilis must be excluded.

Malarial dysentery, usually due to subtertian infection, has rather characteristic symptoms, well described by Manson-Bahr as follows:—

"The onset is sudden, and is accompanied by pyrexia and a rigor, and it may be by vomiting. During the course of this the patient is seized with violent central abdominal pains, and passes stools composed of blood clots and bright blood-stained mucus. The stools may not exceed six in the twenty-four hours. They are composed of red blood corpuscles in rouleaux and columnar epithelial cells; pus cells are absent. This fact alone should make one suspicious that the case is not one of bacillary dysentery.

"Of course a blood slide will reveal the presence of the subtertian parasite, both in the ring and crescent stage. The spleen may, or

may not, be enlarged according to the length of time the malarial infection has existed. There is something in the look of the patient that should make one suspicious, the sweating and icteric tint of the sclerotics and skin.

" It is essential that one should be on the look-out for these cases, for unless promptly diagnosed and treated with quinine they may prove rapidly fatal."

It is important to remember the possibility of malarial dysentery as these cases may find their way into a dysentery ward where malaria is not suspected and routine blood smears are not taken.

Complications.—Intestinal gangrene, peritonitis, eye affections, arthritis, rheumatic symptoms and polyneuritis may be mentioned. The last named, which may be associated with œdema, tends to pass off as the ulcerations heal up. An acute suprarenal syndrome has been described.

In true dysenteric arthritis it is usually the larger joints such as the knees, elbows, etc., which are attacked. This complication, which is often monarticular, must be distinguished from the polyarticular arthritis which so frequently follows the administration of anti-dysenteric serum. In this latter form, which is due to the foreign protein contained in the large bulk of serum given, and *not* to the dysentery, the smaller joints of the hands and feet are specially attacked, although almost every joint in the body may be affected. Serum arthritis is transient and rarely lasts more than two or three days.

Prognosis.—In untreated cases it may be said that the immediate prognosis is worse than in untreated cases of amœbic dysentery, and the late prognosis better as there is no risk of tropical liver abscess.

If promptly and properly treated bacillary dysentery quickly clears up. If neglected or wrongly treated there is often no more distressing and rapidly fatal complaint.

Prophylaxis.—In the main this is the same as that for amœbic dysentery. Carriers exist as in typhoid and are troublesome. Patients with bacillary dysentery should, wherever possible, be isolated, and not treated in the same ward with other patients.

The chief drawback in the past to the use of anti-dysentery vaccines has been their toxicity due to the virulent exotoxin produced by Shiga's bacillus. Chemically detoxicated prophylactic vaccine has given encouraging results experimentally, but no opportunity has arisen of testing its efficacy on any large scale.

Treatment.—*Medicinal and General.*—Absolute rest in bed is important, for if the infection is due to Shiga's bacillus the heart muscle may be damaged by the potent toxin. Prior to the introduction of sulphaguanidine the most generally effective medicinal treatment consisted in the administration of salines by the mouth which assist the body in its efforts to get rid of the invading organisms and their toxic products. The following mixture will be found serviceable :—

Sod. (or magnes.) sulphat.	gr. 60
Acid sulph. dil.	min. 15
Tinct. zingiber.	min. 5
Aq. menth. pip.	ad ½ oz.

Commence with a double dose of the above, and continue with single doses given every hour, or every two hours, for the first day. On the second day, if the patient is going on well, a dose every three or four hours may be sufficient. Continue the salines in diminishing dosage for a week. If at the end of this time the diarrhœa has not been checked recourse may be had to bismuth carbonate (1–2 drachms in milk, ter die) or to a charcoal and kaolin mixture. It is a mistake to continue with salines for too long. A preliminary dose of castor oil is a favourite practice, followed by salines in 60 grain doses. The desired elimination may also be obtained by means of small and repeated doses of calomel (gr. $\frac{1}{10}$–$\frac{1}{4}$), especially in cases of bacillary dysentery which do not respond to salines.

The treatment of this disease has been revolutionized by the use of sulphaguanidine.

The initial dose should be 0·1 gramme per kilogramme body-weight, then 0·05 g. every four hours until the stools are down to five or less daily. The dose can then be reduced to 0·05 g. eight-hourly continued for at least a further seventy-two hours. The bulk of the drug passes unchanged into the large bowel, where it is free to exert its bacteriostatic action. Sulphaguanidine being a sulphonamide derivative necessitates precaution being taken against toxic effects by the administration of adequate fluid and periodic examination of the blood. Clinically, the response to the drug is shown by :—

1. A feeling of well-being within twenty-four to forty-eight hours of commencing the drug with rapid relief of abdomen pain and tenderness, and the consequent lessening or disappearance of abdominal symptoms.
2. A reduction in the temperature and pulse rate which often reach normal in one to three days.
3. A remarkable reduction in the number of stools : often within five to six days the bowels do not act more than once or twice daily.
4. Rapid disappearance of blood from the fæces with a more gradual reduction in the mucus present.

The earlier this treatment is commenced the more rapid will be the recovery. Nevertheless, in a series of chronic cases where this drug had not been given before the 21st day, and often very much later than this, the results were good, 75 per cent. showing complete healing of the colon.

It is important that the initial doses shall be adequate, but with this proviso: in mild cases a total of 70 to 80 grammes may be sufficient to bring about a cure.

If sulphaguanidine is not available other sulphonamides may be tried. Good results are reported with sulphapyridine in doses as small as 0·5 g. by mouth four-hourly.

Bacteriophage by the oral route has been tried in a number of different localities, but the opinions on the results of the treatment are most contradictory.

If pain and want of sleep threaten to exhaust the patient's strength, do not hesitate to give morphia.

Simple lavage of the lower bowel is very comforting, unless, as is often the case, the bowel is too sensitive to allow of this. A sup-

pository of cocaine gr. ½ and iodoform gr. 3 may afford relief, and also make irrigation easier.

It is in bacillary dysentery, more especially in those cases where the stools become serous, that intravenous saline infusion as for cholera, *and begun sufficiently early*, is likely to be very efficacious. The usual amount is 3 or 4 pints, to which the appropriate dose of anti-dysenteric serum may be added (*see* below).

Some advocate 25 per cent. solutions of glucose in distilled water given intravenously. They are said to act better than salines.

Serum.—In Shiga infections serum may act like a charm provided it is given early, if possible within the first twenty-four hours. Every hour's delay lessens its effect, and if it is withheld until the intestinal mucous membrane is extensively necrosed, no benefit will follow its use. It is doubtful if serum does any good after the third or fourth day. Intravenous injection of concentrated refined Shiga anti-toxin in a dose of 50,000 to 100,000 units should be given in fulminating toxic cases; it is a most important adjunct to sulphaguanidine therapy. This unitage can be obtained in less than 10 c.cm. of serum when purified by means of proteolytic enzymes. It has the additional advantage of causing practically no serum reaction.

The *diet* requires special care. In acute bacillary dysentery plain milk should be avoided; indeed, withholding all food for forty-eight hours is often beneficial if the patient is encouraged to drink as much water or rice-water as possible. In severe cases injections of saline or glucose will have been commenced by this time. Then follow on with such articles of diet as chicken tea, meat extracts, albumin water, barley water, tea, etc., in 6–10 ounce feeds, given at intervals of one-and-a-half to two hours. In accordance with the patient's progress, and as indicated by the tongue and stools, this diet is increased cautiously with the usual gradations of eggs, arrow-root, milk puddings, fish and so on. Solids must be added slowly and with great care, as too rapid increase of diet may cause a sudden and severe relapse.

Treat *chronic cases* by lavage of the large bowel. Eusol is suitable, starting with one or two pints in a dilution of 1 ounce to the pint of water, and increasing the quantity and strength daily. Carefully graduate the diet, making systematic naked-eye and microscopical examinations of the stools so as to gauge the patient's power of digestion and absorption. Few people chew their food sufficiently, and in chronic dysentery the symptoms may be kept going and aggravated by careless mastication. Patient and unwavering insistence on this point may result in an almost incredible improvement in the patient's condition. Yatren (*see* Amœbic Dysentery) may do good, and it is a wise precaution to give small doses of thyroid and other active glandular extracts, especially to women patients. Contrary to what would be expected, injections of anti-dysenteric serum sometimes have a remarkably curative action, possibly by inducing a mild degree of protein shock.

In chronic cases which have become marasmic, the administration of glucose solutions (5 to 10 per cent.) will often be found beneficial. They may be given subcutaneously or intravenously up to 1,000 c.cm.

The arthritis of bacillary dysentery is best dealt with by aseptic aspiration, the application of Scott's dressing, massage and hot air treatment.

Fig. 35.


1
2
2a
3
3a
4
4a
5
5a
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
0
10
20 μ

Flagellate Diarrhœa

The more important flagellates of the human intestine are shown in Fig. 35. The only one of these which is generally regarded as pathogenic is *Giardia intestinalis*. Its habitat is the upper part of the small intestine, and at times it appears to be the cause of a persistent and troublesome diarrhœa. On the other hand, *Giardia* may be present in enormous numbers without causing any symptoms whatever. Do not forget, as has been mentioned already, that *Giardia* may hide the presence of the less obvious *Entambœa histolytica*.

Manson-Bahr considers that the presence of *Trichomonas*, *Embadomonas*, *Chilomastix* and other flagellates in the stools, and therefore in the bowel, in large numbers, denotes an unhealthy condition of the mucous membrane, probably primarily due to some other cause.

Mepacrine in the doses employed for the treatment of malaria will eradicate a *Giardia* infection in many cases, while the symptoms may be relieved by bismuth salicylate, 20 grains thrice daily, or by Stovarsol, 8 grains daily.

Ciliate Dysentery

This is due to *Balantidium coli* (Fig. 35, Nos. 30, 31), but is so rare that it requires no further consideration here.

No specific treatment has yet been discovered for balantidiasis.

Coccidial Infection

Although there is no definite evidence that the coccidia found in the human intestine are pathogenic, it is conceivable that as they are parasites of intestinal epithelium they might become so under certain conditions. Hence, an illustration of the extracorporeal development of *Isospora* is given in Plate 17.

It is probable that *Isospora* may be, under some conditions, athogenic to man as it completes its schizogenic development within the cells of mucous membrane of the intestinal villi which it destroys. It may produce a sub-acute dysentery.

DESCRIPTION OF FIG. 35. (PROTOZOA OF HUMAN GUT.)

(Diagram compiled from various sources.)

All the organisms have been drawn to one scale (shown at bottom of Figure), with the exception of Nos. 30 and 31, which are only half the size of the others. An ordinary human red blood corpuscle on same scale is shown in No. 35 for comparison.

Nos. 1—5. *Entamœba histolytica*

No. 1. Large tissue-invading form, containing five red corpuscles.

No. 2. Small precystic form.

No. 3. Cyst with one nucleus and deeply staining chromatoid body.

No. 4. Binucleate cyst. (Later stage in development.)

No. 5. Mature cyst, with four nuclei.

Nos. 2A—5A represent stages corresponding respectively to Nos. 2—5, but belonging to a strain of *E. histolytica* producing cysts of small size. Such strains are far from uncommon, but the small cysts are frequently overlooked or mistaken for those of *E. nana.*

Nos. 6—9. *Entamœba coli*

No. 6. Large active form, from contents of large intestine. The protoplasm usually contains numerous ingested food-bodies (bacteria, yeasts, etc., from the fæces), but never red blood corpuscles.

No. 7. Smaller precystic form, free from food inclusions.

No. 8. Cyst containing two nuclei. The large clear space is filled, in the living cyst, with a mass of glycogen which stains dark brown with iodine solution.

No. 9. Mature cyst, containing eight nuclei.

Nos. 10—13. *Endolimax nana*

No. 10. Free amœba, with numerous ingested bacteria in its cytoplasmic vacuoles. (Compare the nucleus with those of *E. histolytica* and *E. coli*, Nos. 1 and 6.)

No. 11. Uninucleate cyst.

No. 12. Binucleate cyst.

No. 13. Mature cyst, with four nuclei. (Compare with No. 5A.)

No. 14. Cyst of *Iodamoeba bütschlii.* These cysts are sometimes found in human fæces, and are apt to be mistaken for those of *E. histolytica.* The clear space within the cyst in the figure is occupied during life with a glycogen mass which stains dark brown in iodine solution. The single nucleus is small, and typically in the form of a signet ring. The cytoplasm contains brightly refractile granules, but no chromatoid bodies. (*Cf.* No. 3.) These cysts were originally called " I. cysts " by Wenyon.

No. 15. Small free-living amœba from old human fæces. Amœbæ of this type occur commonly in decomposing organic matter of all kinds, but are never present in *freshly-passed* human fæces. There are many different species, all of which are commonly, though incorrectly, called " *Amœba limax.*" Note the structure of the nucleus, with its large central karyosome. The clear space in the cytoplasm is a contractile vacuole—never present in any of the amœbæ parasitic in man.

No. 16. Cyst of the preceding, with single nucleus, numerous rounded chromatoid masses in cytoplasm, and thick corrugated wall.

Nos. 17—21. **Giardia intestinalis* (=*G. lamblia.*)

No. 17. The free flagellate from the contents of the small intestine. Ventral view, showing the " sucking disc " (for temporary attachment), the two nuclei, eight flagella, etc.

No. 18. Outline of similar form, seen from left side.

* *Giardia* Kunstler, 1882 = *Lamblia* Blanchard, 1888.

No. 19. Cyst from fæces, containing a single individual.

No. 20. An older cyst, containing two individuals formed by division.

No. 21. A cyst with four nuclei (intermediate between Nos. 19 and 20) as it appears in end view. Such cysts may be mistaken for those of *E. histolytica*. (*Cf.* No. 5A.)

Nos. 22, 23. *Chilomastix mesnili*

No. 22. Free flagellate, from large intestine. Note the three anterior flagella, complicated buccal apparatus, etc.

No. 23. Cyst, of typical lemon shape, with single nucleus and remains of buccal structures still present.

Nos. 24, 25. *Trichomonas hominis*

No. 24. Free flagellate, from large bowel, showing undulating membrane, axostyle, etc. Forms with three and five flagella also occur.

No. 25. Degenerate form. The flagellate has lost most of its characteristic structures, and is throwing out a finger-like process, which passes down the body into the dotted positions, and then disappears. This peculiar "undulating" movement may go on repeatedly for hours, or even days, without any change of position occurring.

No. 26. *Dientamœba fragilis.*—A small binucleate amœba which occurs occasionally in man. (*Cf.* No. 2A, 10, 15.)

No. 27. *Embadomonas intestinalis.*—A very small flagellate rarely found in human fæces. It produces a cyst somewhat like that of *Chilomastix mesnili*, but considerably smaller.

Nos. 28 and 29. *Enteromonas* hominis.* The flagellate has three free flagella and one attached trailing flagellum which, however, is sometimes not apparent. It produces a small oval quadrinucleate cyst.

Nos. 30, 31. *Balantidium coli*

No. 30. Free ciliate, as it lives in lumen of gut and in tissues.

No. 31. Encysted form passed in fæces. The cyst figured contained two ciliates, but most cysts contain only one.

Nos. 32—34. *Blastocystis hominis*

No. 32. Large spherical form.

No. 33. Small oval form.

No. 34. Elongated dividing form.

This organism is extremely common in human fæces. It is of vegetable nature and not a protozoon, and is shown here because it is not uncommonly mistaken for a cyst, or other stage, of one of the intestinal protozoa.

---

* Wenyon points out, from an examination of the original preparations, that, as Dobell conjectured, *Tricercomonas* is a synonym of *Enteromonas*.

FILARIASIS

The term filariasis is used here as a convenient label for infection with nematodes of the Order Filarioidea. The genus *Filaria*, regarded in the strict zoological sense, comprises only one species, *Filaria martis*, and is not known to affect man. The species *Wuchereria bancrofti*, originally placed in *Filaria*, has been removed from that genus as its characters do not conform with those of the genotype, *Filaria martis*.

Except for *Dracunculus medinensis* (the guinea-worm), the Filarioidea are of little importance as a cause of military inefficiency. Dracontiasis, as guinea-worm disease is called, is found in many parts of Africa, India, Persia and Brazil ; it was troublesome in certain areas during the last war, notably in East Africa, and is dealt with later.

Wuchereria bancrofti is pathogenic in a certain proportion of infections and may give rise to a variety of clinical conditions such as "filaria" fever, lymphangitis, lymphatic varix, enlarged lymph glands, elephantiasis, chyluria, lymphuria, orchitis, chylocele, funiculitis, abscesses, arthritis, synovitis, chylous ascites, and chylous diarrhœa. The possibility of confusing lymphatic varices with herniæ, plague buboes, or syphilitic infection should be borne in mind. The vectors of the parasite are given on page 32.

Loa loa is carried by several of the Tabanidæ, *Chrysops dimidiata*, *C. longicornis*, and *C. silacea*, in which the larva develops in the thoracic muscles. The parasite is known only in West Africa, and gives rise to fugitive subcutaneous swellings, about the size of a hen's egg, known as calabar swellings, which last for a few days and then disappear, to recur later elsewhere. Occasionally a worm migrates to the eye, causing local irritation and swelling.

Onchocerca volvulus (Africa) and *O. cæcutiens* (tropical America) give rise to subcutaneous fibrous tumours in various parts of the body. The swellings are localized and are easily dealt with by surgical measures. The known carriers are given on page 37.

Dipetalonema perstans (*Acanthocheilonema perstans*) usually produces no symptoms. It is a very common parasite in tropical Africa and is known also in South America. The adults inhabit the mesentery. For the known carriers, *see* page 36.

The embryos (microfilariae) of *W. bancrofti*, *L. loa*, and *D. perstans* are found in the peripheral blood. Except in the Southern Pacific where the vector is a day feeder, the microfilaria of *W. bancrofti* observes a nocturnal periodicity, that of *L. loa* is diurnal in habit, while *D. perstans* embryos are present in the blood both by day and night, although the numbers found vary irregularly from time to time. In examining blood for microfilaria always employ some thick-drop method. If this fails to demonstrate the parasites when

their presence is suspected, add 0·5 c.cm. of blood to 2 c.cm. of the following solution :—

Gentian violet	0·1 g.
Sod. chlor.	0·35 g.
Acetic acid	0·3 g.
Aq. dist.	100 g.

Shake and centrifuge. This fluid will preserve the microfilaria for, at any rate, several months.

Dracontiasis

Dracunculus medinensis.—African and Indian troops are especially liable to infection with dracontiasis, but occasional cases crop up amongst British troops. As already stated, the disease was commonly seen in East Africa during the last war.

The male *Dracunculus* is only about 1 inch in length, whereas the female is from about 1 foot to more than 3 feet long and very slender ($\frac{1}{12}$ inch).

Both male and female live in the connective tissue about the mesentery, and it is believed that, after copulation, the male dies. The gravid female moves downwards apparently in search of water, boring her way head first through the connective tissue of the trunk and leg. Sometimes the movement is towards the arm and hand, very rarely towards the head. Occasionally she presents in the scrotum or penis. Arrived at her destination under the epidermis, she bores to the surface and, as the result of some secretion which she discharges, a small blister forms which betrays her presence. This bulla bursts and a little erosion is visible with a hole at its centre, from which the head of the worm may be seen protruding. Douche with cold water in the neighbourhood of the ulcer, and a clear fluid, soon becoming milky, will be seen to exude. It is discharged from the uterus, the opening of which is near the head of the worm. Examine it microscopically and it will be found full of coiled-up embryos (Plate 18). Sometimes a portion of the uterus itself, in the form of a delicate, pellucid tube, presents through the hole, ruptures, and discharges its contents. This process may be repeated until the uterus is empty and parturition at an end. Repeated douching leads to the same result. If water be added to the fluid, the flattened, sharp-tailed larvæ uncoil and begin to swim about very actively. In muddy water and moist earth the larvæ can survive from two to three weeks, and in clean water for about six days.

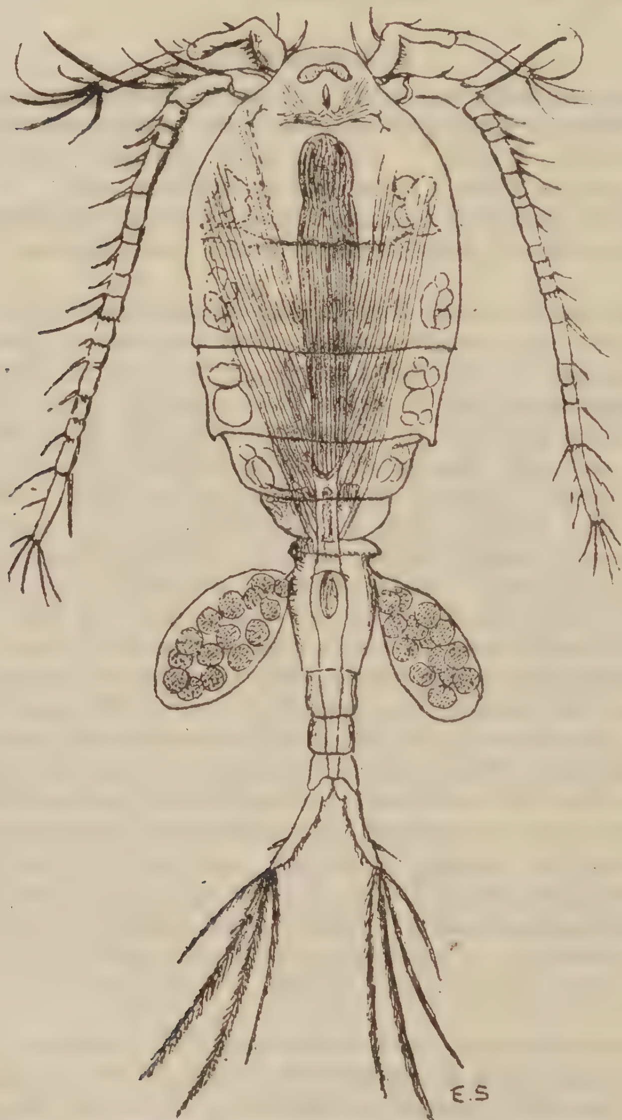
It is of interest to note that in the case of " bheesties " who carry water in dripping skins slung over their shoulders, the guinea-worm often comes to the surface on the back, while in Europeans who bathe frequently the parasite shows itself often on the trunk, scrotum, or thighs.

Having gained the water of a pool or well the larva finds an intermediate host in a small crustacean, *Cyclops quadricornis*, or other species (Fig. 36) which harbours the embryo, and in which it undergoes development for about one month, moulting on two occasions.

After the fourth week the larva does not change, but it can remain alive for over forty days in the cyclops. If this dies the embryo

also perishes. The infected cyclops is swallowed with drinking water and is killed by the gastric juice. The larva breaks out of its dead intermediary host and, probably boring through the stomach wall, finds its way to the retroperitoneal region. As a matter of fact, this part of the cycle is obscure. All we know is that from the time of infection to the time the gravid female worm presents herself a period of about a year elapses.

Fig. 36.



Cyclops coronatus. (After R. Blanchard.)

Symptoms.—Discomfort from the blister and a feeling of weight in the affected limb are usually the only symptoms. Sometimes there are premonitory signs, of which a general or localized urticaria is the most characteristic. A kind of gastric crisis—with gastro-intestinal disturbance, giddiness, and even fainting attacks—has been noted at this stage. Sometimes there is pain and fever, but

chiefly as a result of an accident during treatment (*see* Treatment). There is usually a moderate eosinophilia.

Prophylaxis.—Infected persons should not be allowed in the close proximity of water supplies, wells should be covered and water holes protected. In endemic areas all drinking water should be boiled. Failing this, filtration through cotton cloth will remove infected cyclops, but it must be properly carried out under supervision. Where it can be done the temperature of the water in wells and water holes can be raised by passing steam into them. A temperature of 65° C. is fatal to the cyclops. The addition of a trace of potash to the water is said to be effective.

Diagnosis.—An intradermal test is said to have given positive results in 85 per cent. of cases.

Treatment.—In all cases it is essential first of all to douche the affected part with water until the worm has emptied her uterus of embryos. This will take from fifteen to twenty days. Then if she lies superficially under the skin she may be cut down upon, a broad tape passed round the centre of her body and gentle traction employed for her removal. Even if rupture occurs, no great harm is done in such a case. It is a different matter when the worm is buried in the deeper tissues. Then traction of the living worm (Plate 19), if employed, must be very gradual, carefully and intermittently performed, the worm being wound round a piece of wood or a toothpick. If the worm is broken during the process, abscess formation or sloughing may result. The greatest danger is from septic infection and cellulitis where the parasites lie. This complication is specially likely to occur if the uterus has ruptured and discharged its irritating contents into the subcutaneous tissues. This may take place before or after perforation of the skin has occurred.

Prior to extraction cocaine injections (1 to 3 c.cm. of a 1 per cent. solution of the hydrochloride both into the body of the worm and the tract in which it lies) have been recommended, combined with bicarbonate of soda compresses (15 grammes to the litre). The cocaine paralyses the movements of the parasite and thus facilitates its removal.

The results of treatment by local injections of antiseptics have not been satisfactory, but Mountjoy Elliott has lately reported good results from intramuscular injections of an emulsion of the anthelmintic phenothiazine, especially in the neighbourhood of the buried *Dracunculus*. Extraction of the worm is said to be facilitated.

An injection of 1 in 1,000 adrenaline will relieve the prodromal urticaria immediately. The blister should be aspirated as early as possible so as to limit the size of the subsequent ulcer.

HEAT-STROKE

The term "heat-stroke" is used here to include several pathological conditions of which heat is the principal causative factor. These may be brought about either by a very high atmospheric temperature, or by a lower temperature when associated with a high relative humidity. Mild forms of illness due to heat may be encountered in temperate countries, such as England, during the summer.

Etiology.—The pyrexial or hyperpyrexial form of heat-stroke has been described as "a fever caused by climatic conditions in which the heat regulating mechanism fails to keep the body temperature below the normal upper limit" (Rogers and Megaw). Many experiments and much clinical observation go to prove that there is no mysterious quality in the sun's rays responsible for heat-stroke. The stoker in the boiler room of a liner into which the sun's rays cannot penetrate may fall a victim. Those living high up in the hills in a tropical country, although nearer the sun, do not, owing to the comparative coolness at these higher altitudes, suffer from the effects of heat or fall victims to heat-stroke, whilst those in the sweltering plains below may suffer severely.

In experiments in Manila Aron found that monkeys exposed to a hot sun died within one or two hours. But if the animals were enclosed in large well-ventilated boxes with only the head exposed to the sun, they suffered no harm although the scalp temperature rose as high as 47° C.

Predisposing factors may conveniently be divided into external and internal.

External factors include high relative humidity, especially with air stagnation ; unsuitable clothing and housing ; and deficiency of fluid, food, or salt.

Internal factors are : pyrexia, *e.g.* from malaria or sandfly fever ; gastro-intestinal upsets causing dehydration and salt-loss by vomiting or diarrhœa ; fatigue and want of sleep ; metabolic disturbances, especially from excess of alcohol ; incomplete recovery from a previous attack ; and, in newcomers, lack of acclimatization.

Symptoms.—The clinical varieties of heat-stroke are heat exhaustion and heat hyperpyrexia.

Heat Exhaustion will often overtake heavily-laden soldiers on the march in hot weather, and when the man is relieved of his accoutrements and has a rest he may recover rapidly. The condition, however, is really a syncope, and (like other faints) may progress to prostration, with giddiness, nausea, and a clammy sweat. The pulse is thready, the breathing shallow, and, it may be, sighing, the pupils dilated, and unconsciousness and even death may follow. After recovery headache may be troublesome, and mental confusion and other cerebral symptoms may be noticed.

Heat exhaustion is non-febrile, and indeed the temperature may be subnormal ; but there is danger of hyperpyrexia developing during the next few days unless the patient is adequately treated and kept under favourable conditions.

Heat Hyperpyrexia is always serious. The onset may be gradual. Early warning symptoms include frequent desire for micturition, dryness of the skin, drowsiness, vertigo, headache and intolerance of light, also tingling and cramps in the limbs due to chloride deficiency and dehydration. If it is not treated, the pulse quickens, rapidly becoming irregular, the skin becomes hot and dry and the temperature elevated. Delirium, coma or convulsions may ensue. The actual attack may come on very suddenly.

In addition, *heat-cramp* is seen particularly amongst ships' firemen

in the tropics. It results from excessive sweating and the accompanying loss of salts by the body.

Differential Diagnosis.—Heat hyperpyrexia may closely resemble cerebral malaria with high fever, or may complicate malaria. If there is any doubt, the co-existence of malaria should be presumed, even though no parasites can be found in the blood.

Cerebral hæmorrhage, in which the rise of temperature *follows* the insensibility, and cerebro-spinal fever have been mistaken for heat-stroke.

A most important *objective* prodromal sign of heat-stroke is diminution of urinary chlorides. It is said that the danger mark is reached when 3 grammes or less of chlorides are present in a 24-hours' specimen of urine. Practical use of this fact is made in certain up-to-date oil-fields in very hot countries (Persia and Iraq) where, on urinating, part of the urine is by-passed into a special container and the percentage of urinary chlorides estimated by an electrolytic device. A simple rough test for the qualitative estimation of urinary chlorides consists in adding 5 drops of strong nitric acid, followed by a few drops of 1 per cent. silver nitrate solution, to 5 c.cm. of the patient's urine ; normally, a thick precipitate results ; a slight haze or no change points to greatly diminished or absent urinary chlorides.

Prophylaxis.—Under war conditions this is often by no means easy. In the first place it is essential that due warning of the likelihood of the occurrence of heat-stroke be obtained by the keeping of a careful watch on meteorological conditions. A wet-bulb temperature of 83° F. (28·4° C.) with little or no air movement represents the danger point.

Overloading of troops must be avoided, and as far as possible undue fatigue should be prevented.

Times of marching require careful consideration, and should be selected so that starts are made sufficiently early to avoid the main heat of the day and yet not too early to interfere unduly with sleep. A sufficiency of the latter is of great importance in the prevention of heat-stroke.

Alcohol must be avoided at least during the day (until the sun sinks over the yard-arm), and the skin should be kept clean. Clothing should be loose and easy and afford a maximum of ventilation. Dark or tinted glasses give comfort by protecting the eyes from the glare of the sun's rays.

Excessive exercise should not be indulged in, as the profuse sweating caused thereby, with consequent dehydration and chloride loss, may be the deciding factor in the production of heat-stroke.

Constipation may or may not be a predisposing cause, but certainly it is often a prodromal symptom indicating dehydration, and the use of strong purgatives should be forbidden owing to the loss of fluid and salt they cause.

The men most likely to develop heat-stroke are those who are unwell : a healthy man in hard training can stand up to almost any climatic heat provided he has plenty of water ; and precautions must not be such as to lower morale. It may be possible to establish water-points at centres of traffic and places where troops congregate,

so that they can readily get cold drinks and a sluice down. Also, as loss of salt from the body as a result of excessive sweating is one of the main factors in the production of heat-stroke, its replacement is necessary. This may be effected by the addition of salt to the drinking water in the ratio of 10 grains of common salt to the pint of water. Care should also be taken that there is a sufficiency of salt in the ration, and it is best given with the meat ration when the men are most likely to take it. The main meal of the day should be in the evening during the hot weather.

In addition to camp and barrack heat-stroke centres, and facilities for the treatment of this disease in hospitals, "heat-stroke lorries" have been designed to accompany convoys. Good facilities are needed at hospitals in all hot countries, not only to treat incoming casualties, but also because febrile patients in the wards are always liable to develop hyperpyrexia ; they must be closely watched and immediately treated if deaths from this cause are to be avoided. Tented wards may be particularly hot, but can sometimes be cooled with wet brushwood screens or with fans. In hot weather operations and anæsthetics should be reduced to a minimum. Certain drugs such as atropine (hinders sweating), strychnine (convulsant), thyroid preparations (increase metabolism) and opium are best avoided or reduced to a minimum.

There are individuals with a constitutional inability to sweat. These may have to be retained in hospital throughout the hot season, or, better, sent to the hills until the onset of the cool weather.

Treatment of Heat Exhaustion.—For prostration get the patient into a cool place if possible, lay him on his back, loosen his clothing, especially about the neck, and massage his limbs. If there is collapse give ammonia or camphor and restore his bodily heat by hot applications. A warm bath may do good ; also salt drinks. After-treatment is important.

Treatment of Heat Hyperpyrexia.—The main indications are : (1) Reduce the temperature ; (2) Prevent cardiac failure ; (3) Restore chlorides ; (4) Reduce cerebral congestion if necessary ; and (5) Treat any underlying infection.

Reduction of temperature.—The most efficacious means of reducing pyrexia is by securing evaporation of water from the skin. As Leonard Hill points out, evaporation of water at body temperature carries away 0·59 calorie per gramme, whereas the melting of ice takes away only 0·08 calorie per gramme. Moreover, 70 g. of water evaporated from the skin takes away as much heat as 1,000 g. of iced water used as an enema. Consequently, cases should be sprayed with cold water and kept under a fan. As free circulation of air as possible should be allowed all round the patient both above and below. This condition may be conveniently fulfilled by treating the patient on an iron bedstead covered with matting permeable to air.

It may be impossible to secure sufficient evaporation from the skin in an atmosphere almost saturated, or fans may not be available. In such circumstances, patients whose temperature is 103° F. or over, and who do not respond to other measures, may be placed in a tub of water, the level of which is high enough to cover the body

except the head, which may be supported in a hammock or sling containing ice. Vigorous friction may be applied to the entire body by several persons, ice being added freely to the water.

With any active cooling treatment, the rectal temperature should be taken every minute. When it falls to 102·5° F., remove the patient from the bath or spray and wrap in sheets or blankets, with hot bottles for the trunk and limbs but an ice-bag or other cold application for the head. If perspiration sets in the prognosis is good.

The skin should *not* be rubbed with ice, for this induces vaso-constriction and so delays cooling.

After the attack is over the patient must be closely watched for several days, because the function of the heat-regulating centre has been disturbed and hyperpyrexia may return. If the temperature shoots up again cold applications must be resumed.

Prevention of cardiac failure.—If there are signs of venous congestion venesection (10–20 oz.) will help to relieve the labouring heart and congested brain, often bringing about return of consciousness. Stimulants such as caffeine, strophanthus or Coramine may be given, but strychnine is contra-indicated as it may aggravate the liability to convulsions. If these should occur, they can usually be controlled by venesection, following up with bromides. A rectal enema containing 1 drachm of chloral hydrate has been found useful in quieting wildly delirious cases.

Restoration of Chlorides.—Normal saline may be given as a drink or intravenously. If muscular cramps are prominent sodium chloride should be given by mouth or by intravenous injections of hypertonic saline (120 grains to the pint).

Reduction of Cerebral Oedema.—For unconscious patients who do not respond to treatment, withdrawal of 20 c.cm. or more of cerebrospinal fluid may be beneficial.

Treatment of Infection.—Hyperpyrexia often arises during an attack of malaria, or in the course of some other fever. Malaria should always be suspected, and in case of doubt quinine should be injected intravenously as described on p. 161.

After-treatment.—Treat as for concussion, in a quiet room. Administer bromides or phenobarbitone as required. Later, send to the hills. Severe cases, which includes those suffering from residual symptoms such as intractable headache, inability to sweat, etc., should be invalided home when convalescent.

It is not always realized that a man who has had hyperpyrexia or severe heat exhaustion needs at least three weeks' careful treatment before he is allowed to go about or can safely be sent on a long journey.

HEPATIC ABSCESS

Under this heading only the so-called tropical abscess resulting from intestinal amœbiasis will be considered. With the addition of emetine to our therapeutic armature this condition, at one time the commonest cause of death among British troops in India, should rarely occur.

Far more common to-day than the declared liver abscess is the larval and easily curable stage of amœbic hepatitis. This transition stage, which may be difficult to recognize, usually responds satisfactorily to emetine.

Etiology.—In all probability *Entamœba histolytica* is conveyed to the liver from the base of a dysenteric ulcer as a small embolus. Finding a nidus there it commences to reproduce, and by elaboration of its toxins brings about a tissue destruction which, unless there is secondary bacterial infection, is not a true suppurative condition. Bear in mind that the condition may develop in cases which have *apparently* never suffered from dysentery and may occur many years after an attack of amœbiasis.

Symptoms.—It may be said at once that in any man who has had a history of dysentery, especially if it has been proved to be amœbic, the occurrence of rigors, fever, night-sweating, pain or discomfort in the region of the liver, hepatic enlargement, uneasiness or pain in the right shoulder should suggest hepatic abscess. Remember that only a few of these symptoms may be present, and that they may be very slight, or even altogether absent; but remember also that it is usually safe to confirm a doubtful diagnosis by exploratory puncture with an aspirating needle.

The premonitory symptoms, which it is even more important to recognize, are general malaise, anorexia, foul tongue, irregularity of the bowels, high-coloured urine, irritable temper and insomnia. A little later a feeling of weight and fullness in the right hypochondrium may be present and there is often a dry cough. The temperature is hectic in type; or there may be in rare instances no fever. The haggard look and muddy complexion are very suggestive to the trained eye and a history of uneasiness when trying to lie on the left side is frequently forthcoming. Still later there is often pain, and just as this pain may be referred to the right shoulder, so it may be referred to the appendix. When the abscess is in the left lobe the symptoms suggest gastric trouble. Jaundice is rare. The patient may walk as though he were supporting his abscess with his right arm. Measurements may show a difference of girth on the two sides and enlarged superficial veins are often visible.

Physical examination may also detect rigidity of the right rectus, tenderness and upward enlargement of the liver and crepitations or pleuritic friction at the base of the right lung. Pulmonary auscultation should never be neglected. Neither should a blood examination, the total leucocyte count, and more especially the differential count, being important. There is usually a leucocytosis of low degree, with only a slight relative increase in the polymorphonuclear cells, distinctly less than that which occurs in septic bacterial inflammation. Although the blood picture is not diagnostic in itself, a leucocytosis of say 15,000, with a comparatively slight increase in polymorphs, *i.e.* up to 70 to 80 per cent., is distinctly suggestive.

In the more chronic cases, although the total number of leucocytes may not be increased, a relative leucocytosis may be detected on comparing the red and white cell counts.

Complications.—Rupture into various cavities and organs and

intestinal hæmorrhage may be mentioned. Adhesions between the liver and the base of the lung and diaphragm are common and may prove troublesome later. Lymphatic spread through the diaphragm with a resulting abscess at the base of the right lung is one of the most common complications.

Morbid Anatomy.—All that need be said here is that the favourite site is the superior and posterior part of the right lobe and near its surface, and that though a single abscess is the rule, multiple abscesses are by no means uncommon.

Diagnosis.—When available the X-rays are useful, for they enable the detection of diminution in movements of the right side of the diaphragm, an important early sign of acute hepatitis. They also show the *upward* enlargement of the liver when an abscess is present in the right lobe and may indicate a definite localized increase in the density of the liver shadow and a change of shape if the abscess is pointing, the normal convexity being distorted. Sometimes the abscess bursts into the lung, the pus being coughed up. Its reddish-brown "anchovy sauce" appearance is very characteristic. Occasionally the abscess is completely evacuated via the lung and bronchi, a spontaneous cure resulting. Cure is, of course, more likely to occur if, the condition being recognized, a course of emetine injections is given to aid the somewhat clumsy efforts of nature. Blood examination must not be neglected, for, amongst other things, it may save one from plunging a needle into a leukæmic liver thereby inducing a fatal hæmorrhage. An examination of the stools should never be omitted, for the discovery of dysenteric amœbæ or their cysts at least indicates a course of emetine, and in obscure cases a short course of this drug is justifiable as a diagnostic measure. Finally there remains exploration by the aspiration needle, the outer extremity of which usually swings up and down like a pendulum if the needle has entered the liver.

Differential Diagnosis.—It is impossible here to mention all the conditions from which liver abscess has to be distinguished. Remember, particularly, malaria and malarial hepatitis, basal pleurisy, inflammatory and suppurative states of the gall bladder, hydatid cysts, appendicitis, liver syphilis, tuberculosis, especially perhaps Addison's disease, scurvy, kala-azar and undulant fever. Liver abscess may complicate an infection with *B. paratyphosus* C.

Treatment.—Only the vegetative stages of *Entamœba histolytica* are ever found in the liver, cysts never having been recorded in a liver abscess. The vegetative stage of E.H. is far more amenable to emetine by injection than are the cysts, and it is largely for this reason that most cases of amœbiasis of the liver, even if early pus formation has occurred, are amenable to a relatively short course of emetine injections. Of course, the underlying intestinal condition may necessitate longer and repeated courses. In the pre-suppurative stage, and even apparently when the abscess has actually begun to form, emetine given by the needle may effect a cure. A grain once or ½ grain twice a day should be given. If the symptoms are not relieved, and pus is suspected, needling of the

liver should be carried out. A 20 c.cm. syringe fitted with a wide-bore needle at least 5½ inches long should be employed.

When an abscess is discovered, the condition usually responds well to combined aspiration and emetine treatment. But the aspiration may have to be repeated; and there may be more than one amœbic abscess. Moreover, after successful treatment of amœbiasis of the liver, it may still be necessary to deal with an amœbic infection of the bowel, which may not have caused obvious symptoms. For this purpose, emetine bismuth iodide may be given in 3-grain doses for at least twelve consecutive nights in the dry powder form in a hard gelatine capsule. Carbarsone and stovarsol may also be used, as described on p. 104.

JAUNDICE

Jaundice, a visible staining of the tissues with bile pigments, is a symptom more frequently encountered in diseases of tropical and sub-tropical areas than in western medical practice because of the greater frequency of diseases which cause a high degree of blood destruction or exert their toxic effects upon the cells of the liver or of the reticulo-endothelial system.

Normally bilirubin is present in the blood in a concentration of 1 in 250,000. If, for any reason, the bilirubin increases to a concentration of about 1 in 50,000, it begins to be excreted into the urine, and at about the same point jaundice becomes clinically obvious. This condition of hyperbilirubinæmia may arise in three ways :—

(*a*) *Obstructive Jaundice.*—Obstruction within the bile ducts causes a rise of pressure, and the bile excreted by the hepatic cells is reabsorbed by the hepatic capillaries. This obstruction may occur in the finest bile capillaries, in the medium-sized bile ducts, or in the extrahepatic bile duct system (hepatic duct, common bile duct). The obstruction may be due to causes within the ducts (*e.g.* gall stones) or in the wall of the duct (cholangitis, congenital obliteration), or be due to pressure on the duct from outside (tumour, gumma, hydatid, cirrhosis, etc.).

In obstructive jaundice all the constituents of the bile are retained in the body, viz. bile pigment (causing jaundice) ; bile salts (causing itching and bradycardia) ; cholesterol (causing xanthoma). In addition, absence of bile from the intestine interferes with the absorption of Vitamin K, causing a hypoprothrombinæmia and a consequent tendency to hæmorrhage.

The bile pigment manufactured in the reticulo-endothelial system (largely *outside* the liver) cannot, by reason of the obstruction, be excreted by the normal channels. Consequently, the stools are pale and they are also bulky with excess of fats from malabsorption due to the absence of bile salts. The urine contains abundant bile pigment and bile acids. Bile pigment may be found in the urine before jaundice is evident clinically in the skin or conjunctivæ. The van den Bergh reaction is direct positive.

(*b*) *Hæmolytic Jaundice* is due to excessive destruction of red blood cells, leading to the formation by the cells of the reticulo-endothelial system of bilirubin in excess of the quantity that the liver cells, themselves healthy, can excrete. In consequence, jaundice develops, due solely to hyperbilirubinæmia. Bile pigment is never present in the urine in true hæmolytic jaundice, but only urobilin. The van den Bergh reaction is indirect.

This type of jaundice is seen in pernicious anæmia, acholuric jaundice, severe M.T. malaria, blackwater fever, transfusion with incompatible blood and in the action of the venom of certain snakes.

(*c*) *Toxic Jaundice.*—The essential lesion is damage to the glandular cells of the liver, usually accompanied by damage to the hepatic ducts. The bilirubin carried to the liver cannot be there further elaborated, owing to the damage to the glandular cells, and, owing to the blockage of the ducts, any bile that is formed is obstructed in its escape. Bile pigment is generally present in the urine of cases of this type, but in the later stages urobilin alone may be found. The van den Bergh reaction is biphasic.

This group is a large one and includes the jaundice that may occur in all forms of hepatitis, acute, subacute or chronic, and the causative agencies are very varied. These may be classified as :—

A. Chemical.
   1. Organic—trinitrotoluene, tetrachlorethane, carbon tetrachloride, chloroform, alcohol and cinchophen.
   2. Inorganic—arsenic, phosphorus, gold.

B. Organismal.
   1. Bacterial—typhoid, especially paratyphoid B, typhus, pneumonia, septicæmia and pyæmia.
   2. Spirochætal—syphilis, relapsing fever, Weil's disease.

C. Virus diseases, as yellow fever, and probably epidemic infective hepatitis.

D. Unknown agencies, as in eclampsia, some cases of acute yellow atrophy, and possibly some classified as catarrhal jaundice.

With this very varied etiology the degree of damage to the liver cells and the degree of associated primary or secondary cholangitis is very inconstant and the intensity of the jaundice, the amount of bile in the urine and the colour of the stools may vary within wide limits.

Where jaundice is a symptom of diseases discussed elsewhere in these Memoranda reference should be made to the appropriate section. The remainder of this section is devoted to two conditions in which jaundice is the predominant symptom, and in which no specific etiological agency has been identified.

Catarrhal Jaundice.—Cases occur in all climates of sporadic "catarrhal jaundice" said to be associated with a catarrhal gastro-duodenitis which causes œdema at the mouth of the common bile duct and in the ampulla of Vater, and with exudation of thick mucus, consequent obstruction of the duct. The onset is usually associated with gastric symptoms, anorexia, nausea and sometimes vomiting, which precede the jaundice by a few days. The van den Bergh

reaction is a prompt direct positive, and such cases are generally considered truly obstructive and catarrhal in origin. This condition affects chiefly adolescents and young adults, and lasts for a variable period, perhaps a week or two, after which the jaundice gradually fades. A light diet, rich in carbohydrate and poor in fat, is usually prescribed, along with a morning saline, and recovery is the rule.

There are also encountered cases which, although apparently sporadic, show evidence of a toxic agency. The liver is often found to be tender and enlarged, and the van den Bergh reaction is of the biphasic type commonly found in cases of toxic jaundice. Occasionally in Great Britain, and more commonly in other countries, temperate as well as tropical, small localized outbreaks of jaundice of this type are met with, individual cases being clinically indistinguishable from the sporadic catarrhal jaundice mentioned above. There is a growing trend of opinion towards considering these to be of a toxic type due to a communicable infection probably with a virus.

Recent investigations in Denmark by means of aspiration biopsy of the liver have shown that in twenty-six cases of *sporadic* jaundice in which staining appeared a few days after the onset, biopsy a week after the appearance of jaundice revealed a diffuse hepatitis characterized by inflammatory changes in the connective tissue with a majority of mononuclear cells, by destruction of the trabecular structure of the liver and by necrotic disintegration of the parenchyma cells in irregular foci and by proliferation of connective tissue in the portal system and diffusely in the lobules. The jaundice in these cases varied in duration from three to twelve weeks and the jaundice subsided with restoration of normal liver structure in a month after disappearance of the jaundice. The cause in these cases was considered to be a virus, probably conveyed by pork.

Epidemic Infective Hepatitis.—Whether or not there is a truly catarrhal (obstructive) jaundice as distinct from a sporadic infective (toxic) type, there does occur a definite epidemic jaundice of the toxic variety, best designated epidemic infective hepatitis, which is of great importance in troops because of its long duration and consequent prolonged stay in hospital.

The disease is most commonly seen in children and young adults, though older people are by no means exempt. It is common in Egypt, Palestine, Syria, Iraq and Malta.

Etiology.—No specific organism, bacterial or spirochætal, has been isolated. The incubation period is a long one—four weeks or longer—while the period of infectivity by the normal routes is probably short. The serum of a patient, however, is probably infective, and the occurrence of cases of the same symptomology and pathology following the use of the earlier sero-vaccine against yellow fever is considered to have been due to the unwitting inclusion of the serum of such individuals in the preparation of the vaccine. The accumulated evidence points to a virus cause. Spread of infection is probably by direct contact, perhaps by droplet infection ; in some outbreaks nasal catarrh is a common finding.

Symptoms.—In most cases there are no marked gastric symptoms. The first common early symptom is anorexia, the urine becomes

dark, the stools lighter and jaundice usually appears. In some cases, no frank jaundice may be seen throughout, but the icteric index is always raised and bile can be detected in the urine. The colour of the centre of a weal caused by the intradermal injection of a solution of 1 per cent. histamine will be yellow when viewed through an appressed glass slide as compared with china-white in normal individuals. There are usually headache and asthenia, symptoms of toxæmia and occasionally slight fever. The liver is often somewhat enlarged and tender during the early stages of the disease. In rare cases the jaundice persists and the patient becomes increasingly toxic and dies of liver failure. Sometimes the disease runs a rapidly progressive course, death from cholæmia occurring within a few days of the onset.

Pathology.—Biopsies made on cases of this condition show that, histologically, mild cases grade into the severe, the only difference being the degree of liver involvement. In a few fatal cases it has been possible to demonstrate that the stomach and duodenum were normal, but that the liver showed degenerative changes in the parenchymatous cells with round-cell infiltration in the portal spaces. There was no change in the bile ducts.

Differential Diagnosis.—Epidemic infective hepatitis shows, even in the early stages, a slight leucopenia, with, in some cases, an increase in the large mononuclears. Weil's disease shows a polymorphonuclear increase and a leucocytosis. Yellow fever can be differentiated by the mouse protection test and the characteristic changes in the liver. Glandular fever with jaundice, a rare complication, can be recognized by the higher mononuclear increase and by the Paul–Bunnell test. Other varieties of jaundice—obstructive, hæmolytic and toxic—must be differentiated by careful clinical examination.

Treatment.—There is no specific treatment. Rest in bed and a light diet with extra glucose by the mouth are required. In severe cases, glucose should be given intravenously. The administration of from 5 to 10 units of insulin may assist in the assimilation of the glucose. Hospitalization is about six weeks.

LEISHMANIASIS (KALA-AZAR)

Wherever Indian troops are employed there is a possibility of kala-azar (black sickness) occurring amongst them as isolated cases and it is very apt to be missed unless one is on the look-out for it. During the last war examples of this disease were seen in Europeans in Malta, where infants and young children are specially liable to attack (*Leishmania infantum*). Dogs are often found infected with *Leishmania* in this region and may constitute an important reservoir of infection. The transmitting agent is unknown, but it is thought to be a variety of sandfly (*Phlebotomus*) which bites both dogs and man. It may crop up anywhere in the Mediterranean area, and is found in the Sudan; there is an important focus in the south east

of the Abyssinian border, along the tributaries of the Blue Nile, Darfur district, and parts of East Africa. The importance of this focus is that the disease here does not react to antimony either as tartar emetic or in the pentavalent form. Furthermore in this variety the parasite is much more difficult to demonstrate. Some authorities consider that in this region lymph-node puncture is more likely to be successful than either liver or spleen puncture. Others still hold that spleen and sternal puncture give the best results. Another form of Leishmaniasis, namely, Oriental Sore, receives separate consideration in these Memoranda.

Etiology.—The disease is due to a protozoal parasite, *Leishmania donovani*. It is one of the flagellates, but in man occurs solely as a small ovoid or sometimes nearly spherical organism which, when stained, shows two masses of chromatin, the larger, a nucleus, placed either centrally or peripherally, the smaller, a very definite short rod or dot, the kinetoplast * (Plate 20). It usually stains more deeply than the nucleus. The cytoplasm of the Leishman bodies is often vacuolated. They multiply by fission and may be found crowded together in endothelial cells. Their chief habitat appears to be the endothelial cells of blood-vessels and lymphatics, especially those of the spleen, the liver, the bone marrow, and the skin. They also occur in the blood, inhabiting both the mononuclear and polymorphonuclear leucocytes.

If cultures be made in appropriate media flagellate forms of the parasite develop. The forms in the human body are resting stages of the parasite, while the cultural forms are analogous to those which occur in the insect vector of the disease.

It is almost certain that the disease is transmitted by sandflies of the genus *Phlebotomus*, for parasites ingested by these sandflies rapidly become transformed into flagellates which, by rapid multiplication, fill the anterior part of the stomach and extend into the pharynx, buccal cavity and proboscis. In some cases animals (hamsters) have been infected by the bites of experimentally infected flies, although the experimental infection of human volunteers has so far failed. In India the vector is *P. argentipes*, in the Mediterranean region *P. perniciosus*, and in North China *P. chinensis*. Though viable parasites may escape from ulcers in the intestine, bladder, and naso-pharynx of infected individuals, it is very doubtful if these bring about transmission of them except possibly on a very small scale, although hamsters have been experimentally infected by the oral route.†

Symptoms.—The disease may have a sharp onset, or may begin indefinitely. In the former type of case, the initial fever may suggest enteric, though usually there is not the same degree of prostration as in that infection, and the tongue remains clean and the appetite good. Or, the fever may be intermittent, and if accompanied by rigors, malaria is simulated.

---

* This is the term originally applied by Alexeieff to the corresponding body in *Bodo*. As Wenyon points out, there is no evidence that the structure is a nucleus.

† Leishmania will develop to the flagellate stage in the body of the bed-bug under experimental conditions, but there is no evidence to show that this insect transmits leishmaniasis under natural conditions.

Again, the onset may be insidious, and in such instances a patient with a history of a few days' illness may show enlargement of the spleen indicative of an infection of several months' duration.

Whatever form the fever assumes, its most characteristic feature is a double remission in the twenty-four hours. This is often evident on a four-hourly chart, but in doubtful cases three-hourly records should be kept. After the usual morning drop, the temperature remains low until the middle of the day, and then rises during the afternoon. Towards evening it drops, but rises again during the night, and falls towards morning. Such is the usual course.

After some two to six weeks of fever, a period of complete or partial apyrexia supervenes with amelioration of the symptoms, but thereafter the fever returns, probably more remittent in type than before. Then apparent improvement again sets in, only to be followed by another relapse.

The vast majority of kala-azar patients show enlargement of the spleen, and usually of the liver also. The spleen enlarges more rapidly (and is not so hard and therefore less easy to palpate) than the spleen of chronic malaria. At first these organs may return to their normal size during an apyrexial interval, but eventually the enlargement becomes permanent. It has been pointed out that the spleen takes about one month to reach the costal margin, and enlarges approximately at the rate of one inch a month, so that a spleen two inches below the costal margin indicates an infection probably of three months' duration. Occasionally the liver is more markedly involved than the spleen. The blood shows a marked leucopenia, the decrease chiefly affecting the polymorphonuclears, with a relative increase of the lymphocytes. In making a differential blood count, probably no eosinophiles will be seen, unless there is a superadded worm infestation, in which case the eosinophile count usually rises to that of a normal person. Within a month of onset some appreciable drop in the white count is to be expected. Later, counts of about 2,000 per c.mm. are common, and in advanced cases the white cells may be reduced to 1,000. There is an accompanying anæmia, relatively less marked than the leucopenia, and the proportion of white and red cells may be 1 : 1,200, or 1,500 instead of the normal 1 : 600. The colour index is not affected.

As the disease progresses, various symptoms may manifest themselves, such as epistaxis and other hæmorrhages, dyspepsia, etc.; but the most characteristic feature, in the later stages of the disease, is the huge spleen, which renders the abdomen protuberant so that it contrasts markedly with the emaciated face, the thin chest and stick-like legs and arms. In Europeans, the peculiar earthy-grey colour of the skin, with pigmented areas surrounding the mouth, on the forehead, temples, etc., is very striking.

In untreated cases the condition drags on its weary course for months and even years, becoming eventually a low continuous fever, or the patient dies from exhaustion or some intercurrent malady such as pneumonia or cancrum oris.

Complications.—Phthisis, pneumonia, cancrum oris and other septic infections, diarrhœa and dysenteric symptoms may be mentioned. Persistent cough is not uncommon.

Occasionally *L. donovani* gives rise to non-ulcerative papillomatous nodules of the skin. These have been noted in persons who have undergone treatment for kala-azar, and at a time when they appear to be free from any visceral involvement. Cases of kala-azar with skin involvement have been noted with special frequency in Northern Sudan, where, of one series investigated, the organism was isolated from various skin lesions in more than 50 per cent. of cases. As a result of the relative frequency of the skin involvement and infrequency of the organisms in the peripheral blood it has been suggested that, in this area, infection has probably occurred via the skin, and not the blood. Gland punctures, which were positive in every case in the above series, support the above hypothesis.

In marked cases of the nodular type of post-kala-azar dermal leishmaniasis affecting the face the differential diagnosis from leprosy may present difficulties.

Diagnosis.—This can only be made with certainty by the discovery of the parasite, either in the peripheral blood in spleen juice obtained by puncture, or by the recently introduced sternal and lymph-node puncture. These are safer proceedings than spleen puncture, but of less diagnostic value (of one series examined by Napier 75 per cent. were positive by sternal puncture, 90·8 per cent. by splenic puncture). Sternal puncture should, in view of its relative safety, always be done first ; if negative, splenic puncture may then be performed with the usual precautions.

Sternal puncture can conveniently be performed with a Salah needle, introduced with aseptic precautions under procaine anæsthesia. The needle may be inserted over the lower end of the manubrium sterni. On striking the bone it is directed towards the patient's head at an angle of 30 degrees to the surface of the bone, and is bored in with a semi-rotatory motion. When the needle has entered the marrow cavity the stylet is withdrawn and 0·25 c.cm. of marrow fluid is sucked out with a dry syringe. This fluid, which looks like blood, may be expelled into a small tube containing potassium oxalate (2–3 mg. per c.cm.). The needle is removed and the puncture wound sealed with collodion. A wide-bore flat-bevel lumbar-puncture needle is sometimes employed instead of a Salah needle.

Splenic puncture gives good results, but is not wholly free from danger. With proper technique and due precautions it is a perfectly justifiable procedure, but it should never be undertaken until a blood examination has been made and all chance of leukæmia excluded. An ordinary all-glass 2–5 c.cm. syringe with a clean sharp needle 1½ inches long will be found satisfactory. If a smear only is required the syringe should be absolutely dry, but if it is proposed to culture the material the barrel of the syringe should contain a few drops of citrate solution. The patient should be directed to inspire deeply and then hold his breath until the needle is withdrawn. A preliminary breathing drill is useful. The operation is simplified if an assistant is available to fix the lower margin of the spleen. Pierce the skin quickly at an oblique angle to the surface, then alter the angle of the needle to about 45°, and enter the spleen in an upward and outward direction, that is to say in the long axis of the organ, to a depth of an inch or a little more.

Withdraw and release the plunger several times until some material from the spleen is seen mixed with the citrate solution, and as quickly as possible remove the needle from the spleen. The spleen substance in the needle should be used for making smears, and that in the barrel of the syringe for culture. In the hope of minimizing the danger of hæmorrhage, patients should be given two doses of calcium lactate gr. 30 during the twelve hours preceding the operation, and a similar amount immediately after. Serious damage to the spleen is most likely if the suspected case is not one of kala-azar. Liver puncture is not advised ; it is of considerably less diagnostic value than spleen puncture and no safer.

Very often the first object to catch the eye during the search for parasites is the deeply stained, rod-shaped kinetoplast. As one looks at it the outline of the ovoid *Leishmania* and its nucleus become apparent.

The importance in diagnosis of a blood culture in appropriate media must be mentioned. The tubes are incubated at 22° C., and the water of condensation examined for flagellates on the tenth day. If negative, the tubes should be observed for at least another ten days before being discarded. It is claimed that the parasites can be grown from the blood in 100 per cent. of untreated cases of kala-azar, but a well-equipped laboratory and first-class technique are necessary. Similarly, tubes may be inoculated with some of the spleen juice withdrawn for microscopic examination, and such cultures may show flagellates when no organisms were found in the spleen smears. Successful cultures have also been obtained from the urine.

The aldehyde test, carried out as follows, is often useful. About 5 c.cm. of blood are withdrawn from a vein and allowed to stand until the serum separates. To 1 c.cm. of the serum in a test tube one drop of commercial formalin is added, the tube well shaken and placed in a rack at room temperature. " If the blood is from a well-established case of kala-azar, three to four months or more, the serum will immediately become viscid, within a minute or two will have ' set ' so that the tube can be inverted without the serum being spilled. . . . Within three to twenty minutes, the time varying in different cases, the whole of the serum will have become absolutely solid and opaque, like serum coagulated by heat or the white of a hard-boiled egg. . . . This reaction may be taken as absolutely diagnostic of kala-azar."

Diseases other than well-established kala-azar (three to four months' duration, or more) may cause a doubtful serum reaction, the most important of these being advanced tuberculosis and leprosy, but Napier and Muir state that in these conditions the serum is never both solid and completely opaque. The test may also be positive in trypanosomiasis.

Chopra's antimony test is said to be more delicate than the aldehyde test and appears somewhat earlier in the disease (two months after onset).

The test is carried out as follows : The serum from 1 c.cm. of venous blood is diluted with ten times its volume of doubly distilled water and placed in a miniature test tube ; a 4 per cent. solution of urea stibamine is then run slowly down the sides of the test tube

with a clean capillary pipette. A positive result is shown by a heavy flocculent precipitate forming immediately; this settles as a flocculent mass in half an hour. A fine granular precipitate which settles more slowly, but forms a compact mass at the bottom of the test tube, denotes a doubtful positive. No precipitate denotes a negative result.

Neither the aldehyde test nor Chopra's antimony test are of proved value in the differential diagnosis of the Sudan variety of kala-azar. The former is often negative in established cases of the disease and is frequently positive in Egyptian splenomegaly.

Differential Diagnosis.—Leukæmia, chronic malaria, tuber culosis, Banti's disease, and idiopathic tropical splenomegaly are the conditions most likely to be confounded with kala-azar, but in certain places undulant fever, trypanosomiasis and ancylostomiasis with enlarged spleen have to be excluded. In the early stages it may be confused with typhoid or paratyphoid and, when more advanced, with abdominal tuberculosis or malignant disease. It must be remembered that the disease may occur along with malaria.

Prognosis.—Until quite recently this was distinctly bad, although the disease was by no means invariably fatal. The introduction of antimony has, however, greatly altered the outlook.

Prophylaxis.—As we do not know with certainty how the disease is spread, it is not easy to recommend an efficient prophylaxis, but, so far as epidemic kala-azar is concerned, experience has shown that it should be treated like any other communicable disease by isolation of the sick, disinfection or destruction of dwellings and fomites, the inculcation of cleanliness both domestic and personal, the improvement of housing conditions, with, as special measures, removal to a new site and the destruction of infected animals such as dogs.

In endemic regions special precautions should be taken to guard against the bites of *Phlebotomus*, and the breeding places of these insects located and attacked.

Treatment.—The established treatment for kala-azar is intravenous administration of antimony, most effectively as one of the pentavalent compounds such as Neostibosan (von Heyden 693), Stibosan, urea stibamine, stibamine glucoside (Neostam), etc. The first-named preparation is highly efficient; it is stable, and when dissolved with aseptic precautions, the solution requires no further boiling. It is given intravenously, dissolved in distilled water in a strength of 1 to 5 per cent., but it is simpler to give the required dose dissolved in 10 c.cm. of distilled water, or in the same quantity of a 5 per cent. solution of glucose. It may also be given by intramuscular injection in a 25 per cent. solution. By whichever method it is given, 0·2 g. may be given for the first injection, and 0·3 g. for subsequent injections, administered every other day.

Cure may be obtained with a total of as few as ten injections, but each case must be judged on its merits, and treatment continued, in the absence of symptoms of intolerance, until the clinical symptoms suggesting cure are apparent. These are :—absence of fever, increase in weight, disappearance of anæmia, rise in the white cell count, and reduction of the splenic enlargement. The strongest

evidence pointing to a cure is a negative result of a spleen culture. Recently, a new pentavalent antimony preparation named solustibosan, suitable for intramuscular injection, has been introduced. The dose varies from 2 c.cm. to 6 c.cm., given on alternate days.

For urea stibamine and stibamine glucoside, Napier recommends 0·1 g. as an initial dose, 0·2 g. as a second dose, and 0·25 g. for each subsequent dose.

Children are tolerant of antimony. As regards Stibosan the following dosage is recommended : One-and-a-half to three years, 0·1 g. ; six years, 0·15 g. ; fourteen years, 0·25 g. If intravenous medication is impossible, Stibosan may be given in 0·1 g. doses into the gluteal muscles (not subcutaneously) in a 5 per cent. solution. Some pain is to be expected, and for this reason injections should not be repeated at the same spot.

Prior to the introduction of the more effective pentavalent compounds, antimony tartrate, either the sodium or the potassium salt, was relied on for treatment, and is still sometimes employed. The salt selected should be dissolved in freshly distilled water, or preferably, in 5 per cent. glucose, and may be given in a 1 per cent. or 2 per cent. solution. Sterilization may be effected by autoclaving for ten minutes at 110° C., or by gently boiling. Very high temperatures are said to cause disassociation of the salt. The solution must be free from any trace of deposit or opalescence, for the development of fungi may split up the tartrate molecule and precipitate the antimony in a toxic form. Consequently the solution used should always be freshly made up. If for any reason this is impossible, the addition of ¼ per cent. carbolic is said to preserve the solution from invasion. Before giving an injection the outside of the needle should be cleansed from any antimony solution by dipping into boiling water, or wiping with a sterile cloth. When the needle has entered the lumen of the vein, and the operator can satisfy himself of this by drawing some blood into his syringe, the requisite amount of antimony solution is injected slowly. If any escapes into the tissues a troublesome necrosis may result, so that the injection must not be attempted if the needle is not definitely in the vein. The injection may give rise to certain complications—severe coughing, perhaps ending in vomiting ; giddiness ; stiffness in the muscles of the neck and shoulder. If marked, these should be usually taken as an indication to diminish the doses, gradually increasing them again as tolerance is acquired. The appearance of jaundice or albuminuria should be regarded as a signal of danger.

In a well-nourished European, treatment may commence with a dose of ½ grain, gradually increased to a maximum of 2½ grains, provided there are no serious signs of intolerance. If the disease has lasted for some time and the patient is in a wasted state, commence with a smaller dose, say ¼ grain. The injections are given every other day and continued, unless contraindicated, until the signs suggestive of cure, given above, are present. A total quantity of 30 grains may be sufficient, but just as in the case of pentavalent compounds, there is no definite curative course, and larger amounts may be required to effect a cure.

In the Sudan variety, which does not react to antimony, promising results have been obtained with diamidino-stilbene (M.B. 744).

This drug has been given daily or on alternate days in doses of 0·5 to 2·6 mg. per kilo body weight by the intravenous route. A course of fifteen injections of 2 mg. per kilo has been given, repeated after seven days' interval if necessary. The solution should be freshly prepared in distilled water made up to a strength of 10 mg. per c.cm. without heating and administered slowly.

Even the most desperately ill patient may respond to this treatment; but toxic effects are more serious than was at first supposed. The minor symptoms, such as transient loss of consciousness, flushing, nausea, headache, increase in pulse-rate and sweating, usually pass off in a short time. But there are now reports of delayed toxic manifestations, including peripheral neuritis and fatal hepatitis and pancreatitis, appearing after the patient has recovered from the disease. In many of these cases the solution had not been freshly prepared.

It is now suggested that the drug should be given less intensively—*e.g.* on alternate days for not more than a fortnight, followed by an interval of at least a fortnight before starting another course.

The patient's general treatment must not be forgotten, and a nourishing and well-balanced diet is required, together with such tonics as may be indicated.

LEPTOSPIROSIS ICTEROHÆMORRHAGICA

This form of infectious jaundice was formerly called Weil's Disease.

Etiology.—*Leptospira icterohæmorrhagiæ*, or, perhaps more properly, *L. interrogans*, is the causative organism and is found in the blood, urine, cerebro-spinal fluid and bloody sputum. Leptospira is a form of spirochæte in which the spirals are in close apposition and the whole organism in the form of wide flexures, which gives it the spirochætal appearance (Plate 26). Imagine a corkscrew compressed tightly from end to end and then thrown into curves like those of a snake and the appearance will resemble that of Leptospira.

Some authorities consider there is no valid reason to subdivide the group Spirochætacea into many genera and subgenera, such as Spironema, Treponema, Leptospira, etc. Accordingly, they recognize only two genera :—

(*a*) *Spirochæta* (including Leptospira). These are actively motile ; have a non-rigid flexible body with tapering ends ; and do not possess terminal flagella.

(*b*) *Spirillum.*—Actively motile with a rigid, inflexible, spiral body with tapering ends ; possess one or more terminal flagella at each end.

According to this nomenclature there are three species of the genus *Spirochæta* pathogenic to man :—*Spirochæta recurrentis*, the cause of both louse- and tick-borne relapsing fever ; *Spirochæta*

pallida, the cause of syphilis and of that closely allied disease yaws; and *Spirochæta icterohæmorrhagiæ*, the cause of Weil's disease. Of the genus *Spirillum* there is only one species pathogenic to man, *Spirillum minus*, the cause of rat-bite fever.

Rats—both *Rattus norvegicus* and *R. rattus*—serve as hosts, Leptospira being found in the kidneys, urine and fæces. It is believed that the disease was originally an epizoötic in rats, but that these rodents have become immune and now act merely as reservoirs of infection. The portals of entry to the human body are not exactly known, but it is believed that infection takes place both through the naso-pharynx and through skin abrasions, possibly by means of infected food or water. Organisms indistinguishable from this Leptospira have been isolated from pools of dirty water in mines and elsewhere.

Spirochætal jaundice is specially prevalent in Japan, where the causative Leptospira was first isolated from rats by two Japanese workers, Inada and Ito (1914). The disease was also prevalent during the Great War, especially on the Western Front. Recently, outbreaks have occurred in this country amongst certain occupational groups in close contact with rats, such as London sewer workers, Aberdeen fish cleaners, etc. In consequence, spirochætal jaundice is now officially classed as an occupational disease and comes under the provisions of the Workmen's Compensation Act.

A few years ago (1936) a number of cases occurred amongst soldiers in the Aldershot district, most of whom had bathed in the Basingstoke Canal. 25 per cent. of the rats inhabiting the banks of this canal were found to harbour *Leptospira icterohæmorrhagiæ*. Cases have also occurred amongst the troops in Northern Ireland.

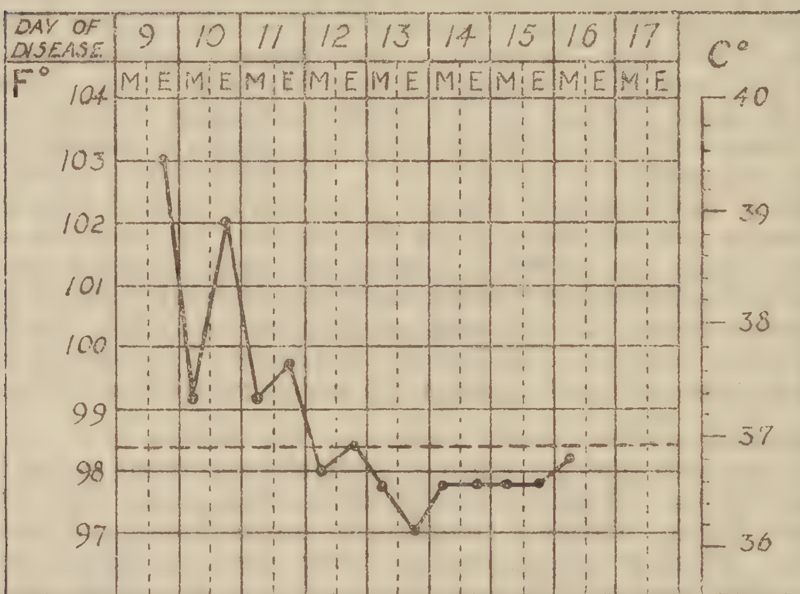
Symptoms.—The general course of the disease is as follows: Onset acute with rigors, vomiting, headache and pains in the head, back and limbs. Muscular tenderness is often acute, especially in the lower limbs. Patients complain of unsteadiness and inability to stand. There is usually irregular fever, the temperature varying between 103° and 105° F. and falling by lysis about the tenth or eleventh day (Figs. 37 and 38). Intense lassitude and severe prostration are common. Jaundice shows itself about the fourth or fifth day of the illness and deepens until the ninth or tenth day, when it fades rapidly. The conjunctivæ are injected and jaundiced. This conjunctivitis (pink eye) occurs in a high percentage of cases and is of considerable diagnostic importance. The colour of the skin is lemon or orange, rarely greenish. Sometimes it has a peculiar hue owing to a combination of yellow jaundice and red vasomotor dilatation of surface capillaries. Pruritus is rare. It is important to note that jaundice may be absent. Rashes—erythematous, measly, and petechial—have been described. The urine is high coloured and nearly always contains albumin, sometimes in large amount and with numerous renal casts. Leptospira may be present in it. The tongue becomes very dry, brown and fissured. Labial herpes is common and the bullæ may be hæmorrhagic.

The pulse is slow in the later stages and the blood pressure low. There is generally a leucocytosis and a differential count in the acute stage shows an increase of polymorphs. Later a lymphocytosis is

found. The fæces are pale and there is usually a good deal of gastro-intestinal disturbance. Constipation is the rule.

The liver may be enlarged, the spleen rarely so. Sometimes the hepatomegaly is sudden and so marked that it gives rise to pressure dyspnœa. The gall bladder is distended and tender on palpation. The superficial lymphatic glands, especially those in the groins and axillæ, are frequently palpable. Other points worthy of note are that in bad cases typhoidal, uræmic and meningeal symptoms may occur. Leptospira may be found in the cerebro-spinal fluid of a proportion of those with meningitis. Hæmorrhagic cases are not common, but are usually dangerous. Epistaxis, hæmaturia, melæna and bloody sputum have been noted. Various ocular changes have

Fig. 37.



Leptospirosis icterohæmorrhagica.
(After Young.)

been observed, chiefly of an inflammatory nature like iritis and irido-cyclitis.

A secondary rise of temperature about the beginning of the third week has been described especially in the older accounts of Weil's Disease.

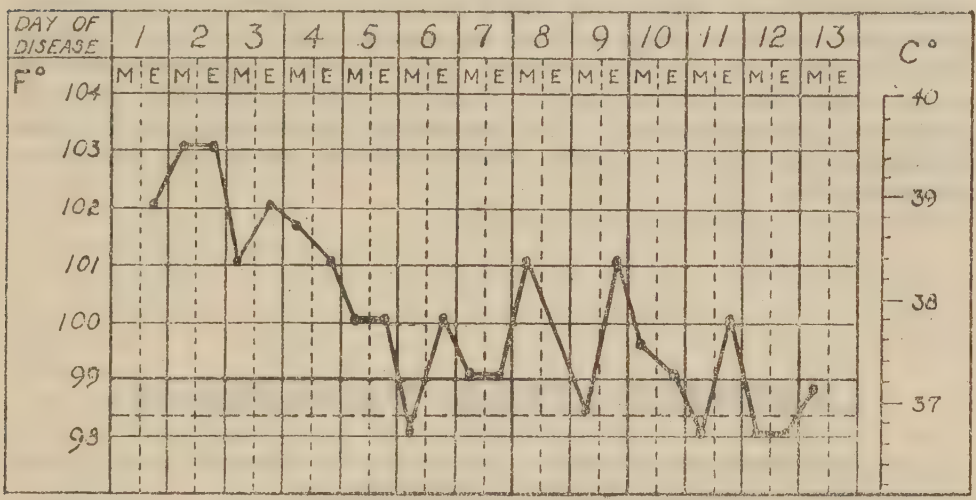
The malady appears to be more severe and more often fatal in hot countries. It leaves behind it a varying degree of anæmia and considerable debility, often rendering the patient ineffective from a military standpoint for four or five months. In some cases a renal sclerosis has been noted.

The disease may vary in intensity from the severe toxic form, just described, to a mild febrile disturbance in which the temperature may never reach 100° F. The intermediate grades of severity may show a few days' fever, continuous or intermittent, with or without

relapses, and sometimes there is a close resemblance to dengue. In all, however, injected conjunctivæ and a trace of albumin in the urine appear to be constant signs. Several serological types of Leptospira have been described, regarded by some authorities as distinct species, but for the present it seems better to regard these as mere variants of *L. icterohæmorrhagiæ.*

Diagnosis.—The Leptospira are present in the blood during the first few days of the febrile period, but are usually few in number, and it is generally necessary to inoculate a guinea-pig to demonstrate their presence. The guinea-pig should be inoculated by rubbing the blood or (after the first week) urine on the shaved or lightly scarified skin of the abdomen. With the urine this should be done at the patient's bedside as the Leptospira rapidly disintegrate in urine that is allowed to stand even for short periods, especially if acid. After the death of the animal they may be seen in large numbers in the liver. After the first week of the disease the Leptospira should be searched for in a centrifugalized specimen of urine. Inada has found that most cases pass spirochætes in the urine after the twentieth day.

Fig. 38.



Leptospirosis icterohæmorrhagica.
(After Ryle.)

The microscopic agglutination test for immune bodies is very simple. It only requires a killed suspension of Leptospira. Dilution of the patient's serum is made and mixed with an equal quantity of the antigen, rocked for ten minutes and read by means of a hand lens against a black background. The titre rises during the first two or three weeks of illness.

Differential Diagnosis.—Distinguish from infective hepatitis.

Yellow fever, cerebro-spinal fever, relapsing fever, plague, rat-bite fever, dengue and several other acute diseases may simulate leptospirosis icterohæmorrhagica. Noguchi probably confused

Weil's disease with yellow fever when he described his *Spirochæta icteroides* (probably identical with *L. icterohæmorrhagiæ* and *S. interrogans*) as the cause of the latter disease.

Prophylaxis.—Disinfect urine, fæces and bloody sputum. Urine may contain Leptospira for several months, generally in small numbers after the fortieth day.

Destroy rats and prevent their access to food (*see* Plague). Prevent insanitary conditions generally, and pay particular attention to water supplies. Protective inoculation with a vaccine prepared from killed cultures of *L. icterohæmorrhagiæ* should be considered in the case of those at special risk (*i.e.* laboratory workers; London sewer workers, etc.).

Treatment.—The specific serum if available should be given without delay in doses of 20–60 c.cm. intravenously, and repeated for several days. Otherwise the treatment is chiefly symptomatic. Flush the patient freely and, if necessary, cup over the kidneys. The condition of the liver would indicate the administration of glucose, at least in bad cases. Ten per cent. solutions may be employed intravenously. The serum of convalescents by the intramuscular route in daily doses of 30 to 40 c.cm. has been recommended.

Hexamine is generally found useful.

LYMPHOPATHIA VENEREUM

Lymphopathia venereum.—Synonyms for climatic bubo, lymphogranuloma inguinale, fourth venereal disease.

This is a widespread contagious disease, usually acquired by sexual intercourse, due to an ultramicroscopic filterable virus, communicable to most laboratory animals. The initial lesion consists of a small often transitory herpetiform lesion on the genitalia or perianal region. This is followed by an inflammatory reaction in the regional lymphatic glands and surrounding connective tissue (climatic bubo in males). If untreated this usually progresses to suppuration with constitutional symptoms, lassitude, loss of weight, pains in the body, sweating and fever. The disease may affect any age or sex, but is more common in the age of greatest sexual desire. It occurs in all races and has a world-wide distribution, but is not very common in England.

Clinical Picture.—The primary lesion is usually on the genitalia. In males the commonest site is the coronal sulcus; in females it may occur on any part of the external genitals. In both sexes the lesion may be near the anus. The characteristic lesion on the genitals consists of a small herpetiform vesicle or ulcer, sometimes multiple, with clean-cut edges, surrounded by a reddened zone, but not indurated and free from pain or itching. The primary lesion is often

small and may escape notice, healing spontaneously. The incubation period is usually less than a week. From this site infection spreads by the lymphatics, which may become inflamed, to the lymph glands into which they drain. In the male, with a primary lesion on the penis, the inguinal glands become involved ; in the female or male with an anal primary lesion the perirectal glands are affected. This glandular swelling occurs within ten to thirty days of contracting the infection. The first local symptom is stiffness and aching in the groin followed by swelling. In the early stages the enlarged gland is discreet and movable but tender. The inflammatory process usually progresses to involve all the inguinal group of glands on one or both sides with considerable periadenitis causing fixation of the mass with involvement of the skin. The mass may be as large as a hen's egg, The adherent skin usually assumes a purplish colour. Spread to the iliac glands causing considerable swelling of this group not infrequently occurs. Untreated, spontaneous resolution may occur, but more frequently the gland mass breaks down at several points with the formation of multiple minute abscesses, which eventually open on the surface at one or numerous points. These fistulæ show no induration and exude scanty viscid opalescent pus free from organisms. The process may progress and untreated continues for months leading to blockage of lymphatics and consequent swelling of the parts drained by these vessels.

The constitutional symptoms vary, but fever, sweating, headache, loss of weight and nausea are commonly present and may persist for a considerable time. Spontaneous improvement however usually occurs after a variable period. There is no characteristic blood change.

Rectal changes leading to stricture more frequently occurs in females. The narrowing is usually situated within 3 to 8 c.cm. above the anus.

Diagnosis.—The clinical picture is usually sufficient to enable a diagnosis to be made, but this should be confirmed by Frei's test. This is carried out by injecting intradermally 0·1 c.cm. of the antigen, which is a saline extract of affected glands, and as a control a similar amount of normal saline on the other side. The result should be read after forty-eight hours. A positive result consists of an infiltrated inflammatory dome-shaped area, 0·5 cm. or more in diameter, which can be felt as well as seen.

There may be a small central area of necrosis and a red zone round the lesion. This test is specific and very reliable.

Differential Diagnosis.—These must be made from other causes of adenitis, such as sepsis, chancroid, syphilis, tuberculosis, carcinoma, Hodgkin's disease and plague.

Treatment.—The disease often responds well to the sulphonamides given in the usual doses. The temperature and general symptoms usually subside in a few days. The adenitis may take a considerable time to clear after all other manifestations of the disease have disappeared. If suppuration has occurred local treatment should be on the usual surgical lines. Excision, however, is usually contraindicated.

MALARIA

Malaria is distributed in the area lying between 63° N. and 35° S wherever there is a sufficiency of mosquitoes hospitable to the germ together with conditions of temperature and humidity which permit the complete development of the parasite in the infected mosquitoes. In these Memoranda it is quite impossible to deal in anything like an adequate manner with what is one of the most common and important of human diseases, but an attempt is made to present a concise account of malaria, special attention being paid to questions of prevention and treatment.

The Mosquito.—Development of malaria parasites has been found to take place in the following anophelines (other than American and Australian species). Those marked "a" are notorious carriers wherever found. Species marked "b" are effective in some part of their range, while those susceptible to infection but not known to be of any epidemiological importance are marked "c":—

b. *Anopheles aconitus*, c. *A. algeriensis*, a. *A. annularis* (=*fuliginosus*), c. *A. austeni*, b. *A. barbirostris*, b. *A. bifurcatus*, a. *A. culicifacies*, a. *A. fluviatilis* (=*listoni*), a. *A. funestus*, a. *A. gambiæ* (=*costalis*), c. *A. hanabusai*, c. *A. hatorii*, c. *A. hispaniola*, b. *A. hyrcanus*, c. *A. jeyporiensis*, c. *A. karwari*, b. *A. kochi*, b. *A. leucosphyrus*, a. *A. maculatus*, c. *A. maculipalpis*, a. *A. maculipennis*, c. *A. marshalli*, c. *A. mauritianus*, a. *A. minimus*, b. *A. multicolor*, c. *A. nili*, c. *A. pallidus*, a. *A. pattoni*, c. *A. pharœnsis*, b. *A. philippinensis*, c. *A. plumbeus*, a. *A. punctulatus*, c. *A. pulcherrimus*, c. *A. ramsayi*, c. *A. rhodesiensis*, c. *A. separatus*, b. *A. sergenti*, c. *A. smithi*, a. *A. stephensi*, c. *A. subpictus* (=*rossii*) a. *A. sundiacus* (=*ludlowi*), a. *A. superpictus*, b. *A. tessellatus*, c. *A. theobaldi*, c. *A. turkhudi*, b. *A. umbrosus*, c. *A. vagus*, a. *A, varuna*.

It must be understood that a species of *Anopheles* capable of carrying malaria may have little or no epidemic importance, by reason of its habits. But it must be understood, too, that the habits of even the same species may not be the same throughout the whole of its range. In Northern Europe, for example, *A. bifurcatus* does not come into houses, and so can have taken little part in the spread of malaria when the disease was common in those parts. Whereas, in Palestine, *A. bifurcatus* haunts houses and is a most important carrier.

It has been recognized during the past few years that within certain species of anopheline mosquito there exist varieties, the individual characteristics of which are indistinguishable except in certain minute respects, and yet which differ markedly in their habits and capabilities of transmitting malaria. For example, *A. gambiæ* var. *melas* is the main vector in Sierra Leone : its habits are quite different from the ordinary *A. gambiæ*.

A. maculipennis, an important vector of malaria, exists and breeds freely in many parts of this country, where indigenous malaria is rare, and also in Holland where it is common, especially in the Northern districts.

This discrepancy in the incidence of malaria in two countries in both of which an apparently potent malarial transmitting species of anopheline mosquito flourishes, was, until recently, difficult to explain.

It is now suggested on strong evidence that this apparent anomaly can be explained in terms of the different *varieties* within the one species of *A. maculipennis* found in the two countries.

In those Northern districts of Holland where malaria is endemic the prevailing variety is *A. maculipennis atroparvus*, which breeds in brackish or salt water, winters in the habitations of its victims and, being only a partial hibernator, sallies forth on its blood-sucking forays from time to time during the winter months when weather conditions allow, each blood meal being normally followed by egg-laying.

The variety common *nowadays* in England, on the other hand, is *A. maculipennis messeæ*, which is, largely on account of its habits, a poor vector of malaria. This variety shuns human habitations, breeds only in fresh water and, being a wholly hibernating variety, is incapable of ovipositing during the winter.

That this relatively harmless variety or sub-species was not always that prevalent in this country is suggested by the well-known fact that malaria (ague) was at one time, not so very many years ago, as common as it is now rare. It has been suggested that a change in the habits and hygiene of our people has also produced a change in the prevailing mosquito fauna, a happy augury for malarial campaigns elsewhere if true.

Four other varieties of *A. maculipennis* (*melanoon, typicus, labranchiæ*, and *elutus*) have been described.

It must be emphasized that the anatomical differences between the above varieties are minute, even inconstant, and in some cases limited to minor differences in the egg floats.

Every medical officer serving in the tropics should make himself familiar with the local anophelines and should lose no opportunity of studying their respective breeding habits and seasonal variations, and try to ascertain the degree of responsibility of each in spreading malaria.

The Parasite.—The four recognized species of malarial parasite pathogenic to man are *Plasmodium malariæ, P. vivax, P. falciparum*, and *P. ovale*. A fifth, *P. tenue*, said to be common in the North East and Central India, has not received general recognition. *P. vivax* and *P. ovale* produce a clinically similar so-called benign tertian fever; *P. falciparum* produces a malignant or subtertian fever; whilst *P. malariæ* produces a quartan fever.

The sexual forms (gametocytes) of quartan and benign tertian, *i.e.* those adapted for life and development in the mosquito, are spherical, while the gametocytes of malignant tertian are crescentic or sausage-shaped (Plate 21).

On reaching the mosquito's stomach the male parasite (microgametocyte) develops flagella (microgametes) which play the part of spermatozoa. These enter and fertilize the female parasite (macrogamete) which is formed from the female gametocyte (macrogametocyte) as the result of certain nuclear changes. The body resulting from this union is known as the zygote, which now becomes motile (ookinete or travelling vermicule) and, penetrating the

stomach wall of the mosquito becomes encysted under its outer limiting membrane to form the oocyst. In heavy infections the outer aspect of the stomach may be studded with oocysts. The contents of these cysts divide to form vast numbers of spicular rod-like bodies, the sporozoites. The oocyst, which has increased greatly in size, finally bursts, and the contained sporozoites are thrown into the hæmocele (the "blood bath" surrounding the intestinal canal of all arthropods, which takes the place of the blood vascular system of vertebrates) and thence find their way to the salivary glands of the mosquito, which is now infective.

The whole process may take about twelve days to accomplish, but the period varies according to climatic and other conditions, and the mosquito may remain infective for many months. When she feeds and injects saliva the sporozoites are carried down the salivary canal in the hypopharynx and into the skin. The immediate fate of the sporozoites is not known. It is doubtful if they penetrate directly into red blood cells. Some hold the view that they first develop in cells of another type (possibly, of the reticulo-endothelial system). Eventually young parasites appear in the red cells; they increase in size, produce and retain, scattered throughout their protoplasm, the malarial pigment, hæmozoin (melanin), and destroy the containing red cells. There is now no question of male and female forms, for multiplication within the human host is non-sexual. Each young parasite within its host cell grows larger and larger until the time has come for it to divide. By this time the parasite, if belonging to the species *Plasmodium vivax* (benign tertian), is so large that it has greatly distended the red cell containing it, which, moreover, has become stippled (Schüffner's dots). These Schüffner's dots, which appear in the parasitized red cell and *not* in the infecting plasmodium, are due to an alteration in the staining reaction of the former due to the presence of the growing parasite (trophozoite) within it and are not excretory products (such as, for instance, hæmozoin) elaborated by the latter. They appear in a proportion of red cells parasitized by all stages of *Plasmodium vivax* beyond the young ring stage (*i.e.* trophozoite, schizont. gametocyte) (Plate 21 *a*).

With quartan and malignant tertian parasites (*P. malariæ* and *P. falciparum*) this enlargement of the host cell does not take place nor do Schüffner's dots appear, although in the case of malignant tertian certain dots (Maurer's dots) may appear within the red cell: these are by no means constant and are best seen in well-stained slides (Plate 21, *c*). In the case of *P. ovale* the red cell becomes stippled (often heavily) with Schüffner's dots and may be oval in shape (hence the name) and the edges may be frayed (Plate 21, *d*). In all cases, however, division takes place, the one original parasite (schizont) dividing into many merozoites, the number varying with the species; quartan and ovale, six to eight; benign tertian, fifteen to twenty-six; malignant tertian, eight to thirty-two. These clumps of merozoites constitute the mature schizont and correspond to a full ripening of the parasite. The membrane of the damaged red cell then gives way and the merozoites are poured into the blood-stream. Some are engulfed by phagocytic white cells, others enter fresh red blood corpuscles and start

again the non-sexual cycle. This process of intra-corpuscular development, *i.e.* from entry to burst, (known as schizogony in contrast to the sexual cycle within the mosquito known as sporogony), naturally takes some time, and the time varies with the species of parasite. In quartan infections it takes seventy-two hours, and in the tertian infections (including ovale) it takes forty-eight hours.

The origin of the different names is now apparent, for stages in the life cycle of the parasite correspond to stages in the clinical picture of the malarial attack. The hot stage with the temperature high is when the parasite is young, and just beginning to grow in the red cell; the fever-free period occurs when the parasite is at least half-grown, and is approaching the stage of division; and the chill with its rise of temperature corresponds to the moment when the red cell bursts and the merozoites are shed. Thus, as the quartan cycle occupies seventy-two hours, the temperature rise takes place on the fourth day (hence the name quartan), while in a simple tertian infection, taking forty-eight hours for its cycle, the rise is on the third day. The same should be, and sometimes is true of a malignant tertian, but too often its pyrexia is quite irregular, being sustained or remittent, while quotidian forms are recognized.

These interesting facts are best realized by a study of the diagrams shown in Figs. 39, 40, 41.

It is well to remember that there occur mixed infections and also what are called subintrant infections—where one attack comes on before the other has subsided. This is due to a lack of uniformity in the developmental periodicity of the infecting parasite or to double or triple infections with the same species of parasite. These greatly alter the characteristic temperature waves.

Various complications may occur, some of them, like coma, intimately associated with the life cycle just described; for it should be mentioned that while the whole life cycle of the quartan and benign tertian parasites takes place in the peripheral blood, this is very rarely the case in malignant tertian infections where schizogony usually occurs in the internal organs, such as the capillaries of the brain, which become blocked with the infected red cells.

A hiatus has yet to be filled in our description of the parasite. It will be remembered the account began by mentioning sexual forms (gametocytes) in the blood. These are formed from the ordinary parasites of the non-sexual cycle. Certain of these become what is called sexually differentiated. Instead of proceeding in the usual way to schizogony they change within their host cells either into special spherical (quartan and benign tertian) or crescentic (malignant tertian) forms. Male and female spheres and male and female crescents are thus produced and the sexual differences can be detected by the trained eye (Plate 21, 5). These are non-febrile forms. They resist quinine and mepacrine to a greater or lesser extent, M.T. crescents being very resistant, the spherical gametocytes of *P. vivax* and *P. malariæ* much less so, and their sole function is to carry on that sexual cycle in the mosquito which has just been briefly described. The gametocytes of all four varieties (especially the crescents of *P. falciparum*) are highly susceptible to pamaquin.

Symptoms and Diagnosis

Symptoms.—It may be said at once that at the outset of many malarial attacks, and in the case of most sub-tertian infections throughout the attack, a definite diagnosis cannot be made in the absence of blood examination.

The incubation period varies, but is often about a week or ten days for malignant tertian and somewhat longer in the simple tertian and quartan types; occasionally the patient develops what appears to be his primary attack of malaria months, perhaps, after returning home from the tropics. In many cases, especially of benign tertian fever, the first clinical attack takes place in the early Spring before mosquitoes are prevalent, presumably the result of infection the previous Autumn.

In many cases the symptoms of a benign malaria infection commence with an initial stage of continued fever lasting for several days without paroxysms, seemingly due to an irregular sporulation of the parasites, terminating by lysis and often followed by a "silent" phase. Thereafter the disciplined febrile attacks of classical malaria occur. In benign tertian malaria, the earlier paroxysms may have a quotidian periodicity, becoming tertian later.

There may or may not be a premonitory stage wherein the patient feels upset, is tired, has an ache in his bones, perhaps a headache, loses his appetite, possibly vomits, and suffers from chilly sensations. At this period his temperature may already have begun to rise, and later on the fever fit fastens upon him. In many cases, however, he finds himself suddenly in the grip of ague, suffering from a definite rigor and such an intense feeling of cold that his teeth chatter and he shivers and shakes.

None of the diseases dealt with elsewhere in this series has such a severe and well-marked onset as is seen in a typical ague attack. Very often the patient begins to vomit violently. He piles clothes upon himself and yet his temperature is elevated, the sensation of cold being entirely subjective. Then comes the stage of heat and febrile distress, with flushed face, rapid pulse, intense headache, frequent vomiting, quick breathing and dry burning skin, during which the temperature often runs up to 105° F. and the coverings are cast impatiently aside. There may be a slight delirium. Anon the sweating stage supervenes, the perspiration pouring from the patient and soaking everything on and about him. The fever rapidly declines and comfort takes the place of acute misery. The patient, though possibly tired, can be, though he should certainly not be, up and about. Then, according to the nature of the infection, one, two or three days later the fever fit recurs (Fig. 42).

It lasts as a rule from six to ten hours, say one hour for the cold stage, three or four for the hot period, and two to four for that of defervescence. The spleen enlarges during the febrile paroxysm and the urine varies according to the stage and may contain albumin.

The above is a classical form of intermittent malarial fever. On the other hand, all kinds of atypical attacks may occur. Relapses of all varieties of malaria are usually more typical, less severe, and more amenable to treatment than the primary attack.

Herpes febrilis, usually round the mouth, occasionally elsewhere,

Fig. 39.—DISEASE—QUARTAN MALARIA.

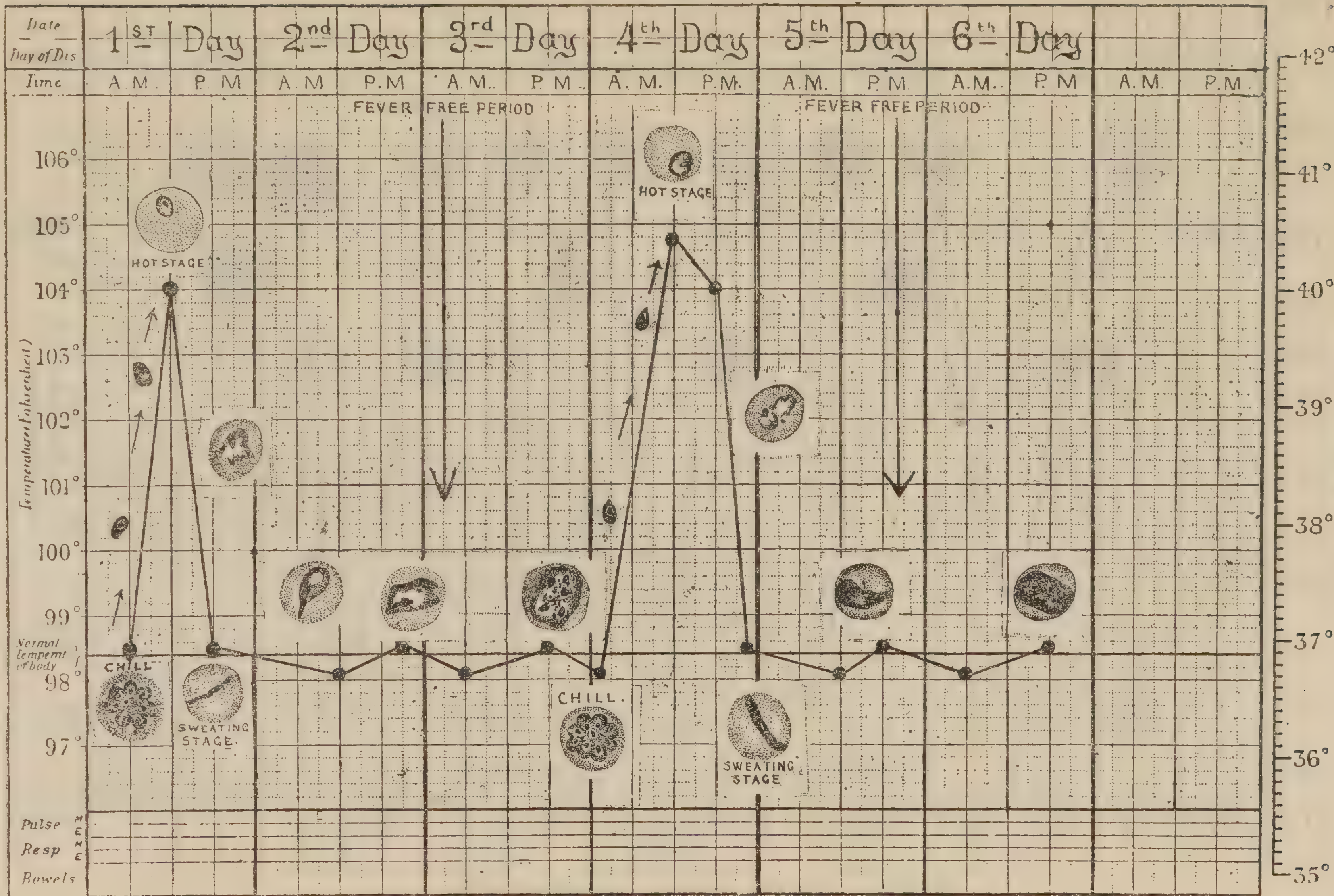


Fig. 40.—DISEASE—BENIGN TERTIAN MALARIA.

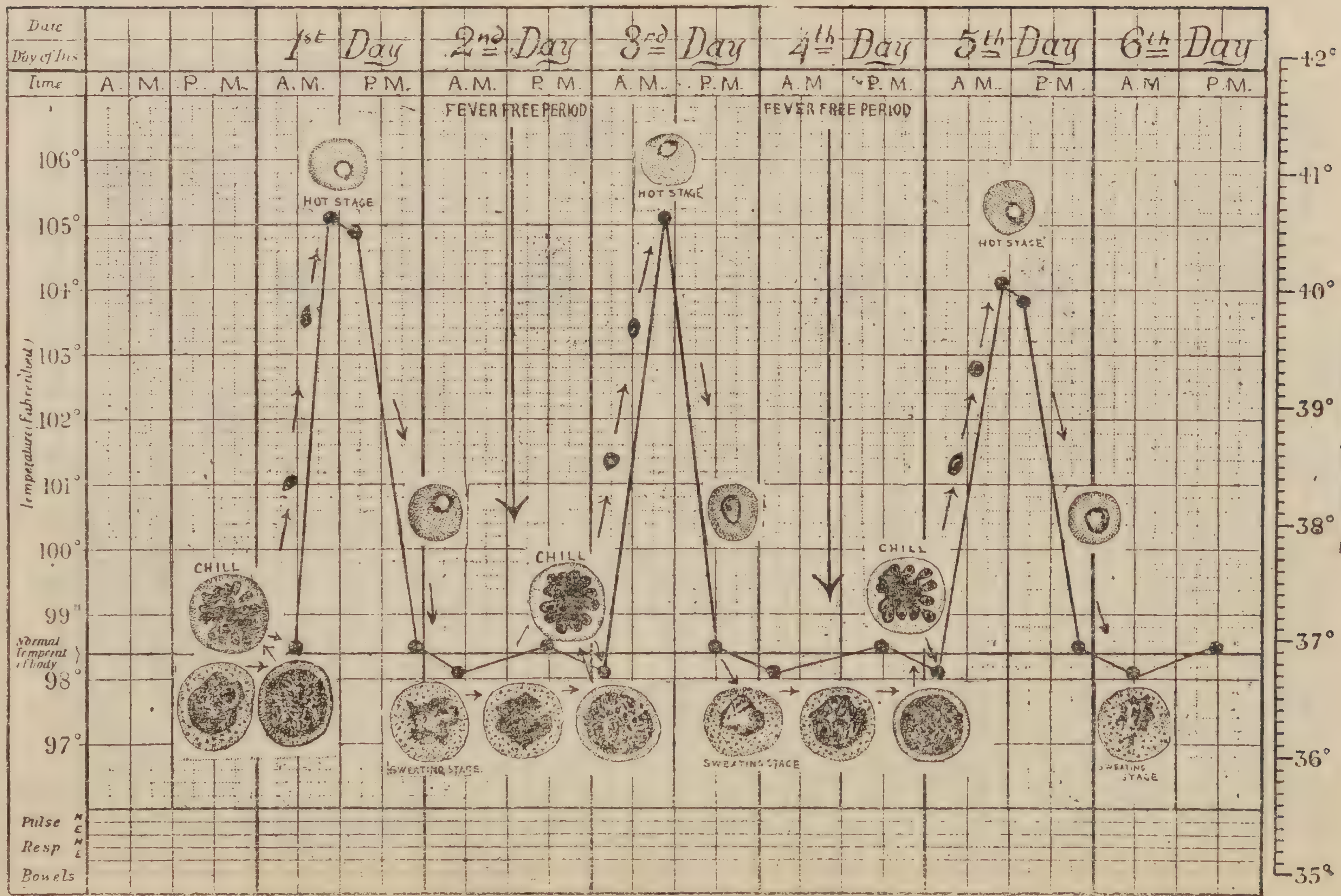


Fig. 41.—MALIGNANT TERTIAN.

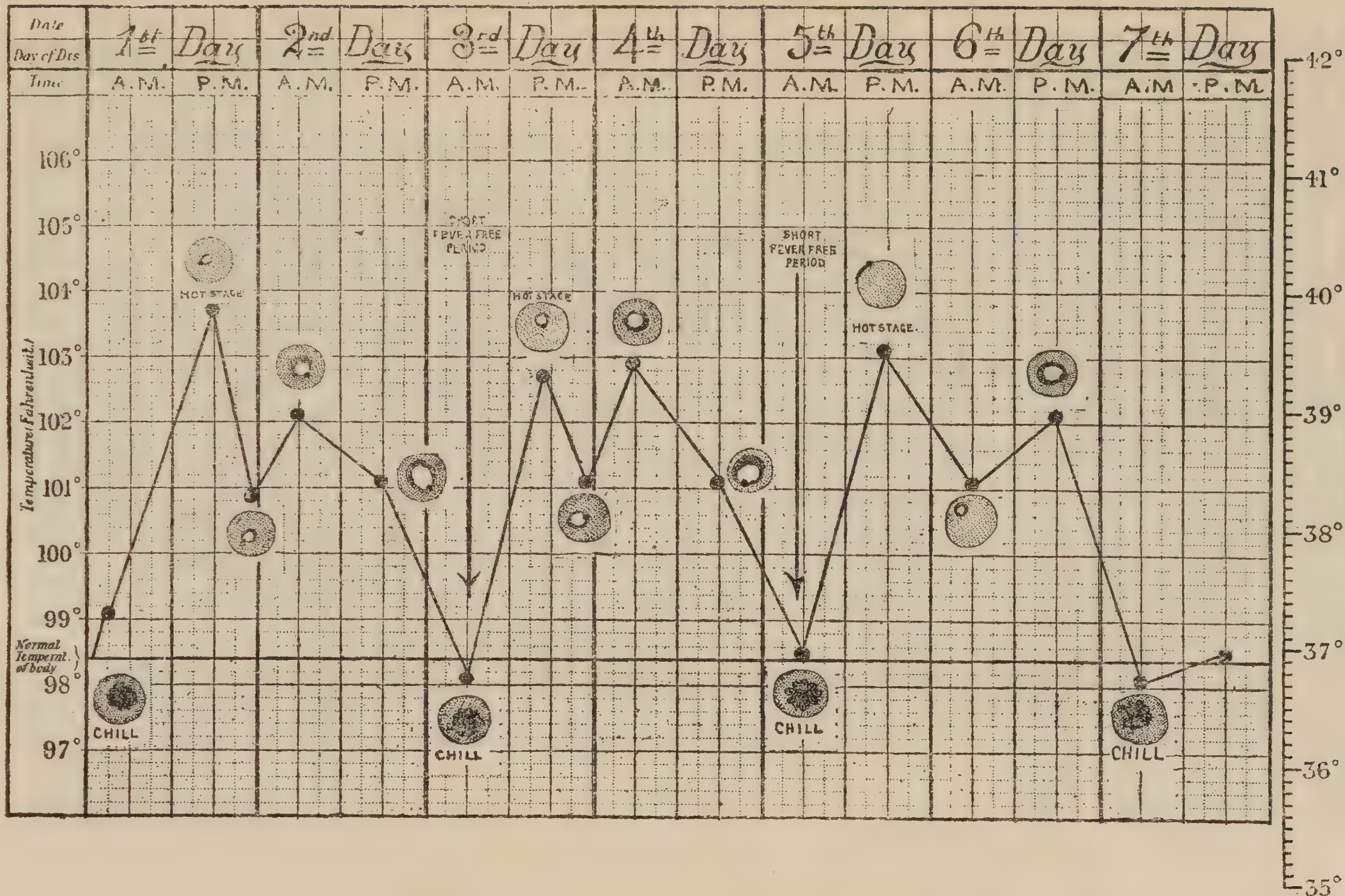
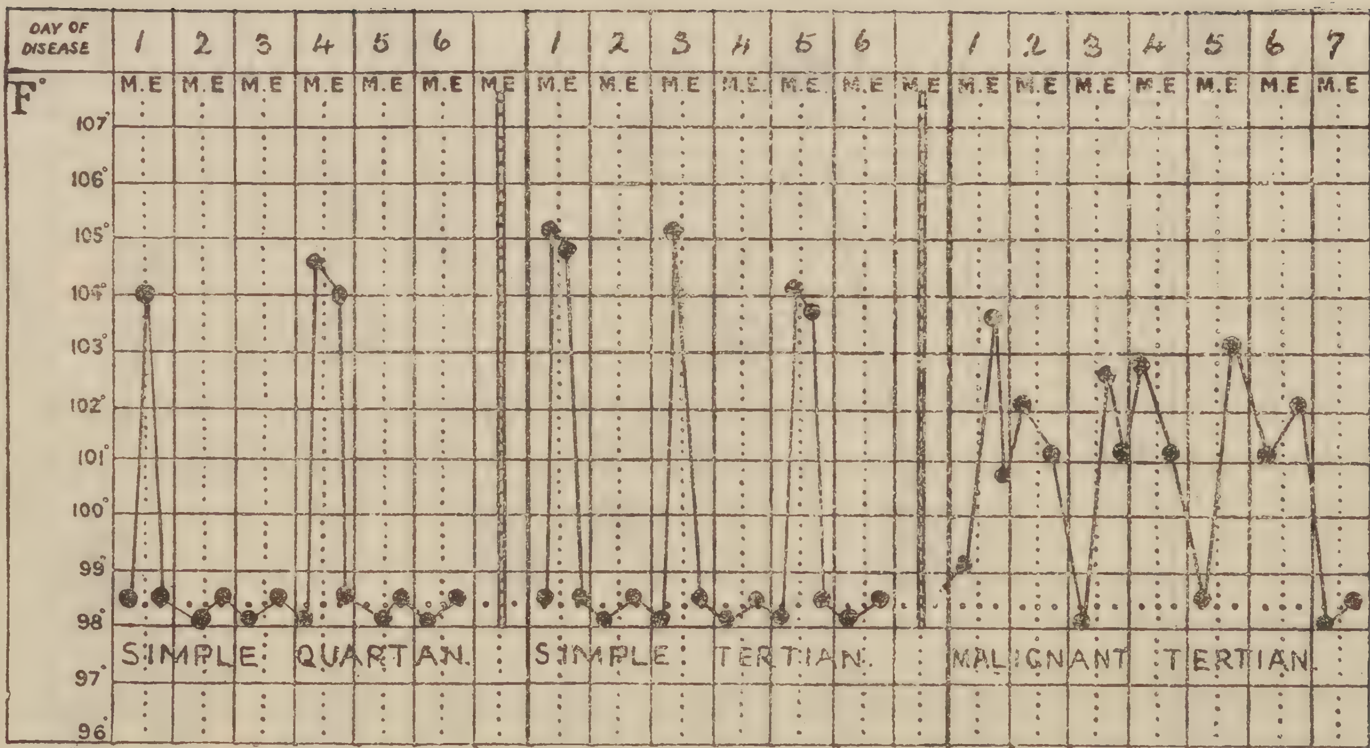


Fig. 42.



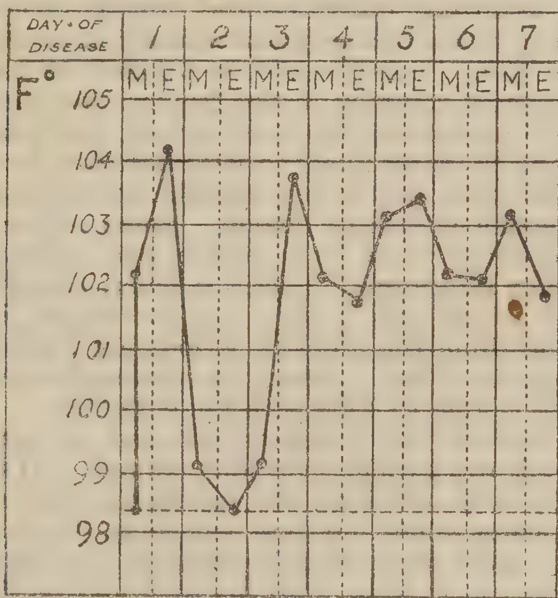
Malaria Charts.

such as on the nose or pinna of the ear, is a common symptom, occurring in about 40 per cent. of cases. Epistaxis is also not uncommon, especially in subtertian attacks.

It should be mentioned that sub-tertian infections tend to be more severe than the others and that the fever is apt to be of a remittent type, so that the alternation of hot, cold and sweating stages is absent or modified (Fig. 43). Further, there are clinical varieties of malaria known as bilious and typhoid remittent, the former associated with jaundice, which are very unlike the ordinary attack. During the last war such cases were most common in East Africa, but were seen also in Macedonia and Palestine.

The occurrence of cerebral, choleraic, dysenteric, hæmorrhagic, pneumonic and syncopal forms must not be forgotten, and as these very fatal varieties are only too often the result of lack of prompt

Fig. 43.



M.T. Malaria showing early tertian fever becoming remittent.

treatment or are due to faulty treatment, the importance of early and correct diagnosis will be manifest. Moreover, if any case of malaria is neglected it may drift into a state of cachexia, which it is frequently as hard to cure as it is to endure and may lead to a protracted convalescence or permanent invaliding.

As regards coma, it should be noted that it may develop quite suddenly, possibly in a convalescent, especially perhaps when he passes from a hot to a cold climate. It may be preceded by delirium and convulsions or come on without warning. Thus it usually resembles either an epileptiform fit or an attack of heat-stroke. The patient cannot be roused to answer questions. He lies and moans. His breathing may be stertorous or quiet. His pupils are often contracted and are like those seen in opium poisoning. His

temperature may be high or, and this is important, normal or subnormal. It is always well to take the rectal temperature in such a case. If not promptly treated he will die. It is important to note that every form of acute cerebral attack may be aped by cerebral malaria. Premonitory symptoms such as very severe headache, photophobia, increased irritability, undue drowsiness, twitchings of the face or extremities, etc., should be watched for. On the other hand, the attack may start abruptly with an epileptiform seizure during the course of an apparently mild malarial attack that has given no special cause for anxiety. Cerebral cases may or may not show a heavy blood infection and a negative blood slide should form no excuse for delaying effective treatment unless malarial infection can be definitely excluded as the cause of the condition. On the other hand, malaria can of course accompany a cerebral catastrophe due to other causes.

The so-called algid type of malaria characterized by collapse, clammy sweat, shallow respiration, subnormal temperature, low blood pressure, vomiting, diarrhœa and lumbar or epigastric pain, has been shown to be due to an intense infection of the suprarenals.

Although the term "malignant" is applied to the sub-tertian variety, which is most common in the tropics, and though it is true that this form of malaria is the most severe, the most exhausting to the patient, and the most likely to terminate fatally or be followed by grave complications, yet it is a mistake to suppose that the so-called benign tertian is always benign. Some of the cases of this class from Macedonia were very severe and caused death with cerebral and other symptoms. Quartan fever, though it induces a very sharp first attack and is very apt to relapse, is not usually serious. For one thing the afebrile periods are longer, for another the number of spores is less. Hence the patient's strength is better sustained and he is able to cope with his parasites.

Spontaneous recovery from malaria can and, in fact, always does occur eventually if the patient lives long enough. If the patient be robust, his phagocytes efficient, the circumstances favourable and the dose of parasites small, he may vanquish the foe and destroy him altogether. More often he only achieves a partial victory, and the enemy retires, as it were, into his dug-outs in the spleen and liver, and his trenches in the bone-marrow, and awaits his chance of making another raid upon the defences. This withdrawal of parasites is what occurs when, apart from actual cure, a malarial attack comes to an end, or when the disease is controlled, though not cured, by treatment. There seems little doubt that these ordinary non-sexual forms remain there, till a chill or some other factor, such as a surgical operation, causes them suddenly to become active and to start reproducing themselves in the red cells, when, of course, up goes the temperature as the rosettes ripen and the red cells burst, and we have all the phenomena of the relapse.

Within the four recognized species of Plasmodium parasitizing man there appear to be many strains which, whilst morphologically alike are immunologically distinct. Those strains which are mutually protective are called homologous strains, whilst those for which no such mutual protection exists are called heterologous strains. For instance, the indigenous adult population of an endemic

or hyperendemic focus of malaria where one strain or homologous strains of, let us say, *P. falciparum* are prevalent may have acquired as a result of repeated infections in their youth complete immunity to that strain or strains. If, however, they are removed to another district where heterologous strains of *P. falciparum* exist, they may suffer from clinical malarial attacks as the result of infection by these new strains against which they have acquired no previous protection. This type of very selective immunity built up as the result of repeated infections with one particular strain or closely allied group of strains depends for its effectiveness on the continued presence within the body of small numbers of the infecting parasites. As long as the parasites are there this immunity, which is called *premunition*, persists; when once the parasites have left the body premunition ceases. This type of immunity is in contrast to that conferred by such diseases as typhoid fever and the exanthemata in which the immunity is of a more "solid" type, not dependent on the continued presence of the infecting organisms within the body. This latter type of immunity which, in the case of malaria is of a more general and less highly specific type than premunition, is uncertain and variable in extent.

Complications.—Coma, due to blocking of brain capillaries by vast numbers of parasite-laden red cells, is the most important. The possibility of the occurrence of blackwater fever must not be forgotten. Dysentery (*see* p. 109), if actually caused by the malarial plasmodium plugging the intestinal capillaries, is an important complication often missed until it is too late. Pneumonia and nephritis merit mention, the latter said to be especially common in quartan infections. Many other complications have also been described, including the severe toxic fatty degeneration affecting the heart and other organs in certain cases of malignant infection. A special form of malarial psychosis has been described, but it is doubtful if such exists as a separate entity.

The possibility of rupture, spontaneous or traumatic, of a chronically enlarged spleen must never be forgotten. Special care should be taken, on this account, in dealing with one's native servants, any one of whom may have his spleen "ripe for bursting".

Diagnosis.—If a typical case be seen at the onset of the cold stage, a history of possible exposure to malarial infection obtained, or indications that the patient may be suffering from a relapse forthcoming, then the pinched appearance, the teeth chattering like castanets, the successive shivers, the enlarging spleen and the elevation of temperature will, even without blood examination, make a diagnosis of malaria well-nigh certain. At any rate, if no facilities for blood examination exist, it is better to give such a patient quinine than to subject him to the discomfort, and it may be danger, of passing through one fever fit and commencing another before coming to a definite conclusion regarding him and exhibiting the specific. Moreover, under these conditions quinine acts as a therapeutic test and by controlling the attack may establish the diagnosis. It would, however, be well, if it were only feasible, in every case of possible malaria infection to have a blood film made and sent with the patient to a hospital where facilities for laboratory

work are provided. In many cases, even when the history suggests malaria, it is impossible to be sure without a blood examination, and, as regards the use of quinine as a therapeutic test, each case must be judged on its merits, and especially has one to consider the probable nature of the infection (whether benign or malignant) and how long it will take before the patient reaches a place where the diagnosis can be clinched.

Outstanding points in arriving at a diagnosis are :—

1. A consideration of all the symptoms.
2. A careful physical examination, more especially of the splenic area, but remember that in early cases, especially if already receiving quinine, or in any mild infection, the spleen may not be appreciably enlarged.
3. The periodicity of the febrile attacks.
4. The result of blood examination.

The paramount importance of the last named was well shown by the valuable results achieved by the advanced malaria diagnosis stations in Macedonia and Palestine. It must be remembered that a single negative examination does not exclude malaria even when the thick film method is employed, as should always be the case.

Malaria tends to occur in most localities in "rushes," during which the medical and nursing staff are worked off their feet. It is therefore necessary for smooth and efficient working that a satisfactory routine be worked out before the onset of the malaria season. Orderlies and nursing sisters should be instructed in the proper taking of thick and thin blood smears as the medical officer will seldom have time to do this himself.

A close liaison must be established with the attached laboratory; arrangements being made beforehand for the rapid notification by phone or messenger of all positive cases. As part of the routine it is advisable to establish a "priority" list, so that slides from patients for whom, for any reason, an urgent diagnosis is required, can be examined and reported on before the routine examinations are made. Unless this is done valuable time may be lost in the diagnosis of urgent cases.

Remember also that many slides, perhaps extending over several days, may have to be examined before parasites are found. This is especially the case in primary infections and in those who have taken quinine, either as a therapeutic measure or prophylactically, prior to admission to hospital. The inhibitory effect of mepacrine on the appearance of malarial parasites in the peripheral blood appears to be considerably less than that of quinine ; indeed there is evidence to suggest that a few doses of mepacrine may have a provocative action, parasites appearing for the first time after one or two days' treatment with this drug (*see* Figs. 46A, 46B).

The vagaries of the disease, the common early stage of continual fever, and the fact that double and even triple infections occur, make malaria difficult to diagnose by clinical examination alone.

Differential Diagnosis.—In this connexion it is instructive to note that cases sent from the Gallipoli Peninsula and definitely diagnosed as malaria by blood examination in Alexandria were

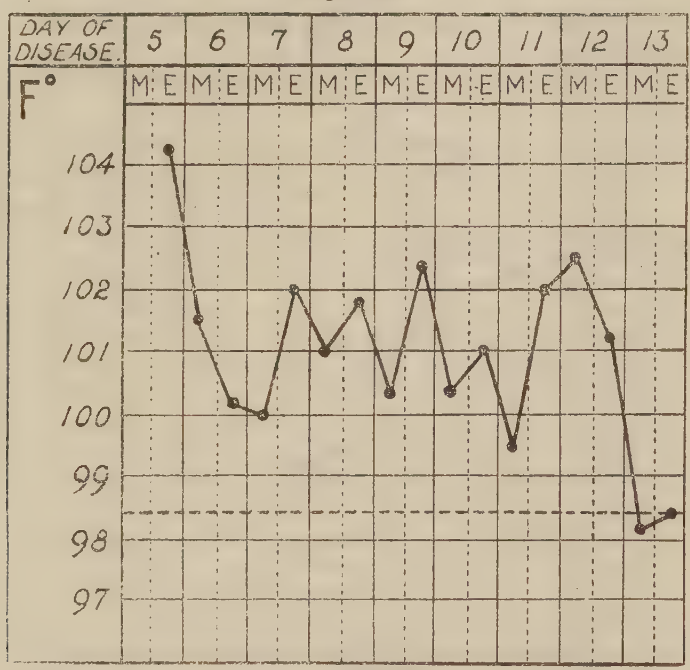
provisionally labelled typhoid or paratyphoid. Influenza and rheumatism were other guesses, and there figured also that refuge for the destitute—simple continued fever. All manner of diseases have been and may be mistaken for malaria or may accompany that disease.

How closely typhoid may resemble malaria and malaria simulate typhoid is shown in a couple of charts (Figs. 44 and 45) which explain themselves, and the milder forms may at the beginning be very like paratyphoid. Further, malaria may run concurrently with either of these infections.

Malaria may simulate almost any acute or subacute fever and may be called on this account "The Great Mimic" amongst diseases.

Malarial coma may have to be distinguished from heat-stroke, cerebral hæmorrhage, uræmia, and alcoholic and opium poisoning.

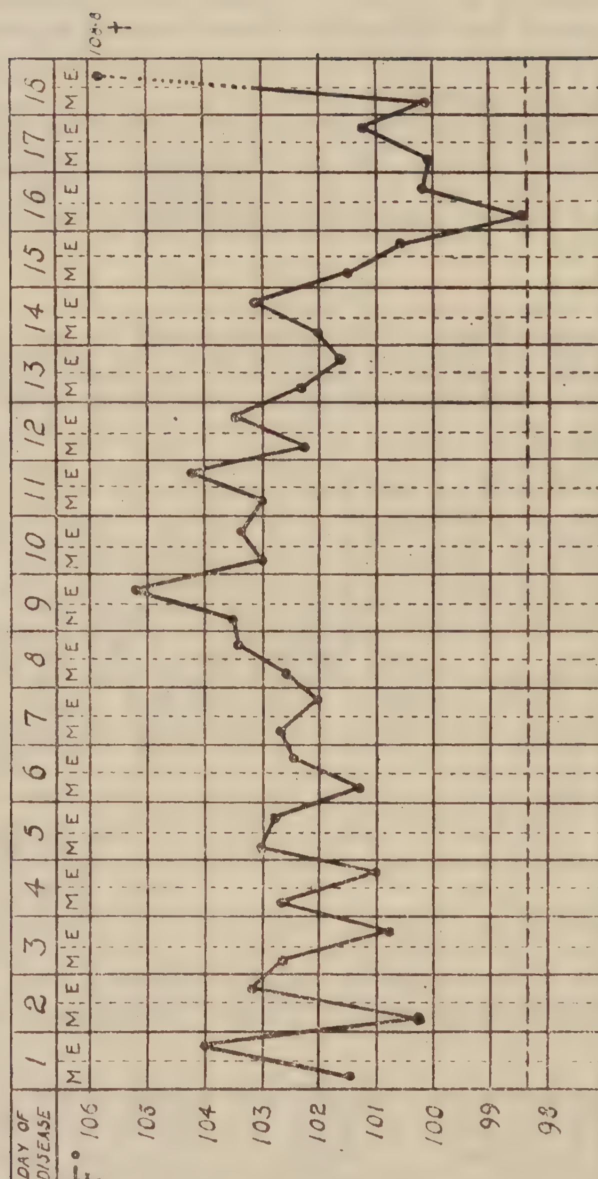
Fig. 44.



Typhoid Fever simulating Malaria. Blood culture positive on 6th day.

If malaria parasites have been found in the blood of a patient whose temperature shows no sign of yielding to quinine within three or four days, test the urine for quinine in order to make certain that the drug is being absorbed into the blood. Proceed as follows :—First test the urine for albumin. If this is absent, add 6 or 7 drops of Tanret's acid solution to 2 c.cm. of filtered urine in a test tube. This should give a dense white precipitate soluble on heating, if quinine is present in ordinary amounts. If the urine contains albumin, add Tanret's solution and boil. Filter while still hot, and as the filtrate cools, the appearance of a precipitate, soluble on further heating, indicates the presence of quinine. To

Fig. 45.



Malaria simulating Typhoid Fever.

avoid any possible fallacy, a patient should not be given other alkaloids or their salts when the urine is to be tested for quinine. Tanret's acid reagent consists of: iodide of potash, 3·0 g.; corrosive sublimate, 1·0 g.; glacial acetic acid, 20 c.cm.; distilled water to 60 c.cm.

Treatment

Objects of Treatment.—Sinton has laid down certain criteria for an ideal treatment of malaria. These are:—

1. It should bring about a rapid cessation of the symptoms complained of and of any acute condition which is likely to endanger life.
2. It should cause no harm to the patient; *i.e.* there should be an ample margin between the therapeutic and toxic doses to allow of individual idiosyncrasy.
3. It should destroy all parasites in the body, or at least bring about such a condition that the natural defences of the body can complete the destruction, thus preventing recurrence of symptoms with reinvasion of parasites into the peripheral blood at a later date.
4. It should rapidly destroy all the sexual forms of the parasite in the peripheral blood and so prevent the patient becoming a carrier of the disease.
5. It should be effective against all the different species (he might have added—against the different "strains" also) of the malarial parasite.
6. It should be cheap (not so important in the case of a military population, an expensive drug, if efficacious, paying for its cost many times over by decreasing hospitalization).

Such a treatment has not yet been found, but in quinine, which is still our sheet anchor, and the new synthetic preparations, mepacrine and pamaquin, if used intelligently and with due regard to their selective action on the malarial parasite and their limitations, we have valuable therapeutic agents which go a long way towards fulfilling the above desiderata.

At the outset it should be noted that malaria in time of war is, in some respects, very different from the disease met with under ordinary peace-time conditions. This is chiefly due to the fact that it is encountered in men subjected to heavy strain and exposure, many of whom are suffering from various degrees of debility and anæmia. They lack the comforts of civilian life, and owing to the nature of their work are liable to more intense infection than is normally the case.

Failure to obtain the desired result may be due to faulty methods of administration of the drug, such as calculated avoidance of treatment or to sophistication of the quinine before or after issue from the store. Quinine bought locally from bazaar shops or elsewhere should always be suspect on this account. A simple test for the estimation of the quinine content of stock mixtures has been devised by Dr. Ghosh and a handy test case is on the market for this purpose.

Then, again, the patient may be unable to absorb the drug in

sufficient quantity, a defect sometimes put right by a sharp purge But if there is any reason, such as the absence of reaction to treatment, to suggest deficient absorption, the urine should invariably be tested for quinine (p. 155). Quinine may appear in the urine within ten minutes of being swallowed, practically always within two hours, but does not continue longer than forty-eight hours after cessation of treatment.

Quinine.—Quinine is one of several alkaloids, all with some anti-malarial action, extracted from the bark of a shrub, cinchona. It is a quinoline derivative of complex molecular structure and may be administered as the base, quinine, or, more frequently, as one or other of its salts, those most frequently employed being the sulphate, bisulphate, hydrochloride, bihydrochloride, and, for children on account of the absence of the bitter taste common to the other salts, euquinine (quinine and ethyl carbonate).

Action of Quinine.—The malarial parasite may be subjected to selective therapeutic attack at various stages of its life-cycle. There is one phase, the sporozoite (the sporozoite is the parasite in its earliest and pre-infective stage, as injected by the mosquito), which has not yet yielded to anti-malarial therapy.

Drugs which attack the parasite at this stage are known as causal prophylactics or sporozoiticides. No true causal prophylactic, effective in therapeutic doses, has yet been discovered.

The schizont stage, the clinical evidence of which is the acute malarial attack, yields to many anti-malarial remedies, of which quinine is probably still the most effective. Therefore, quinine is said to be an effective schizonticide.

Quinine, whilst having some action on the gametocyte stage of *Plasmodium vivax* and *P. malariæ*, causing benign tertian and quartan malaria respectively, has little if any action on the crescents of *P. falciparum* (subtertian malaria); therefore it is a poor gametocide; in other words, its sterilizing power as regards the carrier state is poor.

Relapse Rate.—Exactly what it is that determines relapses in malaria, what happens to the parasites between the relapses, and why some forms of malaria (benign tertian and quartan) are followed by a higher relapse rate than others (subtertian) is not known. Whilst quinine and its salts undoubtedly influence the relapse rate of all forms of malaria to some slight extent, a relapse rate in the neighbourhood of 50–60 per cent. is to be expected if no drug other than quinine is used. This high relapse rate only follows benign tertian and quartan infections. Relapses are less common following subtertian malaria no matter what anti-malarial remedy is used.

Administration.—Quinine salts may be given by the following routes:—

1. Oral.
2. Intramuscular.
3. Intravenous.

Each route has its own clearly defined indications and technique of administration.

Certain other methods of administration, such as rectal, subcutaneous, etc., are seldom used and will not be further discussed.

Oral Administration.—Quinine is best given as a *mixture*, the sulphate being the cheapest, most suitable, and most generally used salt for routine use. It is a mistake to recommend one of the more soluble salts such as the bisulphate or the bihydrochloride on the plea that it is, on account of its greater solubility, more easily absorbed, since all salts of quinine, however given, are reduced to the base in the duodenum before absorption into the blood stream.

Suitable mixtures for routine administration are :—

Quinine sulphate	gr. 10
Dilute sulphuric acid	min. 10
Water	to 1 oz.
	1 oz. t.d.s.

or

Quinine sulphate	gr. 10
Citric acid	gr. 30
Mag. sulph.	gr. 30–60
Water	to 1 oz.
	1 oz. t.d.s.

The individual dose should seldom exceed gr. 10 and the daily dosage gr. 30.

Quinine should always be given, where practicable, as a mixture in preference to tablets or powder. It is found only too often that tablets, especially of the sulphate, are passed unchanged in the fæces.

If, for any reason, tablets must be given, one of the more soluble salts such as the hydrochloride or bisulphate is preferable.

Whereas, formerly, it was the practice to give prolonged courses of quinine extending over several weeks or even months, with the mistaken idea that relapses might thus be prevented, or at least their incidence materially decreased, it is now realized that such prolonged courses influence the relapse rate but little.

The modern practice, sponsored by the Malaria Commission of the League of Nations, is to administer quinine in adequate dosage (*i.e.* gr. 30 daily) during the acute phase, usually for a total of 7–10 days ; this may be followed by a short course of pamaquin (*see* under pamaquin) ; a further quinine course followed by pamaquin being given for each relapse as it occurs.

An alternative to the above, especially useful when bodies of troops are undertaking active operations in highly malarious districts, is to follow the initial quinine course by a course of mepacrine 0·4 gramme per week for at least two months.

Quinine, administered by the mouth, is rapidly absorbed in the vast majority of cases, and this is undoubtedly the best routine method of administration and should invariably be used in the absence of the special indications noted below for intramuscular or intravenous administration.

Intramuscular Injection.—The bihydrochloride of quinine (Rogers recommends the bihydrobromide) is the salt usually used on account of its solubility (1/1 in water).

8–10 grains are dissolved in 2–4 c.cm. of sterile water and injected deep into the muscles of the buttock, care being taken not to inject the drug in the region of the sciatic nerve. Any part of the buttock that can be seen when the patient is sitting is free from this danger: this does not mean to say, of course, that the patient should sit up to receive his injection ; he is usually too ill for this to be safe or, indeed, possible.

The chief indications for intramuscular administration may be tabulated thus :—

1. Quinine cannot, for any reason, be swallowed.
2. Retention of quinine swallowed is doubtful owing to nausea or vomiting.
3. Failing a satisfactory response to treatment, quinine cannot be demonstrated in the urine and its absorption is doubtful.
4. A heavy blood infection, especially important in subtertian infections ; *i.e.* more than 6 parasites per thin field of a blood slide ; even in the absence of a severe clinical attack of malaria.
5. In all severe, especially *pernicious*, malarial attacks.

In addition to the above well-recognized indications it may be advisable, in some areas where subtertian infections are known to be unduly severe, to give *all* cases infected with *P. falciparum*, even if clinically mild and not showing a heavy blood infection, a few preliminary intramuscular injections before proceeding with the routine oral administration.

There are certain drawbacks to intramuscular injection. These may be briefly summarized :—

1. It is apt to be painful. This is not usually the case if properly carried out, rigid asepsis maintained and the sciatic nerve area avoided.
2. It may leave indurations lasting for years.
3. Some necrosis of tissue invariably follows intramuscular injections of quinine. Occasionally, especially in the case of debilitated individuals or if the technique has been faulty, an abscess forms which may lead to extensive sloughing, prolonged invalidism, and even endanger life.
4. Tetanus, due either to autogenous infection or to the introduction of spores at the time of injection, is a rare sequel.

In spite of the above somewhat formidable array of objections thousands of intramuscular injections may be given without ill-effect, and one should never hesitate to use this method if faced with any of the indications mentioned above.

On the other hand, intramuscular quinine should never be used merely as an alternative to oral quinine, nor should it be continued a day after the special indications mentioned above have been brought under control, when the course may be completed by the oral route.

Intravenous Injection.—Quinine is given by the intravenous route when, for any reason, a very rapid concentration of the drug in the blood stream is considered advisable, or if the patient's condition

is considered to be so bad that administration by other routes is unlikely to be followed by absorption.

It is indicated in some of the more urgent pernicious attacks, especially *algid* and *cerebral* malaria, both of which constitute grave medical emergencies.

Some consider that the indications for intravenous quinine are the same as for the intramuscular route, and always give the former in preference.

They claim the following advantages :—

1. Absence of pain.
2. Absence of necrosis of tissue and its sequels, gluteal abscess and prolonged invalidism.
3. Rapid action.
4. Absence of tetanus as a sequel.

The following drawbacks to intravenous injection may be noted :—

1. Intravenous quinine depresses the circulation and may further lower the blood pressure in an already severely shocked patient.
2. Fatalities occasionally directly follow its use.
3. The rapidity of its action may in itself constitute a danger, a large number of parasites suddenly being destroyed and the toxic products of their disintegration thrown into the general circulation (a variety of Herxheimer reaction).

Quinine bihydrochloride is the salt usually chosen for intravenous injection. 8–10 grains are dissolved in 200 c.cm. of warm sterile saline solution and infused into the vein at the bend of the arm ; or the same dose may be dissolved in 20 c.cm. and injected very slowly from a syringe. In collapsed cases an intramuscular injection of 10–15 minims of adrenaline hydrochloride 1/1000 may be given before the intravenous quinine. Adrenaline or pituitary extract should be ready at hand for emergencies. The intravenous injection should be repeated if the patient is still unconscious after 12 hours ; but oral quinine should be instituted directly the special indications necessitating intravenous or intramuscular quinine have ceased to operate.

Other Quinine Preparations.—A number of proprietary preparations, many of them containing a quite insufficient quantity of quinine, are on the market. Amongst these may be mentioned the following :—

Esanophele.—An Italian quinine-arsenic preparation ; each tablet contains gr. $\frac{1}{3}$ quinine bisulphate, gr. $\frac{1}{100}$ arsenious acid, and gr. $\frac{2}{3}$ iron citrate. The adult dose is 6 tablets (containing gr. 2 quinine) daily. Probably on account of its arsenic and iron content esanophele has proved useful in the treatment of chronic relapsing malaria.

Bacelli's mixture.—Contains rather more quinine sulphate which is combined with iron and arsenic. The dose is 30 c.cm. t.d.s. Both the above are popular continental remedies.

Quinio-stovarsol and *quinine troposan* (troposan is an isomer of stovarsol), constitute a convenient method of giving quinine in association with arsenic.

Stovarsol has a definite therapeutic action on *P. vivax* infections, but has little effect on infections due to *P. falciparum* or *P. malariæ.* It has therefore to be combined with quinine as a general therapeutic agent in malaria.

The dose of quinio-stovarsol is gr. 4 (1 tablet) 4 times a day. This contains gr. 8 of quinine.

Tebetren is a proprietary drug containing hydroquinine (closely allied to quinine), acriflavine (an acridine derivative with no specific action on the malarial parasite) and bile salts which are supposed to act as a detoxicating agent.

The active principle of this British preparation is hydroquinine, and its therapeutic indications and limitations correspond closely with those of quinine.

Malarcan has a similar action to tebetren, but contains hydroquinidine in place of hydroquinine.

Cinchona febrifuge is an impure mixture of all the alkaloids present in cinchona. It is considerably cheaper than the quinine salts and is, on that account, suitable for village use. It is very insoluble and is best given as a powder, the dose being the same as for quinine. The drawback of the preparation is that its alkaloidal and quinine contents are not standardized and, whilst some samples are potent, others are almost inert.

Totaquina, a refined modification of the above recommended by the Malaria Commission of the League of Nations, is standardized to contain not less than 70 per cent. total alkaloids of which $\frac{1}{5}$ must be quinine.

Toxic Effects of Quinine.—The administration of quinine is attended with little risk and close medical supervision is seldom necessary.

Certain characteristic side-effects are, however, observed when the concentration of quinine in the blood reaches a certain point. These are grouped under the term, *cinchonism*, and consist of deafness and buzzing or ringing in the ears, slight giddiness and tremors; the first two, especially, occur in a considerable proportion of those taking quinine in therapeutic doses, are of little importance, and subside rapidly when the drug is discontinued.

Rarely, definite idiosyncrasy to the drug is met with, and some few individuals develop an alarming train of symptoms of an allergic type after even small doses (gr. 1 or less) of quinine. These toxic symptoms vary from case to case but include urticaria with marked itching, skin hæmorrhages, dyspnœa, œdema of the eyelids and elsewhere, and dangerous or even fatal collapse.

In the past such individuals have either been debarred from living in a malarious district or have lived there at their peril. Various substitutes were used, notably quinidine, an isomer of quinine, but unfortunately this drug is not free from risk. Luckily, nowadays, we possess in mepacrine an effective and harmless substitute.

Apart from the above, excessive dosage (as much as gr. 180 daily has been given in the past by some misguided enthusiasts) may

lead to permanent blindness due to quinine amblyopia, and to permanent internal ear deafness.

Quinine Resistance.—Some authorities have suggested that certain strains of malarial parasite may become "quinine resistant" after prolonged medication, as the trypanosome has been shown to become resistant to certain arsenical preparations.

There is little controlled evidence to support this hypothesis, and it may be assumed as a working rule that if an attack of malaria fails to respond to quinine, properly administered and absorbed, within a week, no matter how many relapses the individual has had and how often his infecting parasites have been "drenched" with the drug, some other cause than malaria for the prolongation of the fever and symptoms must be sought.

Synthetic Anti-malarial Drugs.—Two synthetic anti-malarial remedies, *mepacrine* and *pamaquin*, both of recent introduction, as well as their numerous imitations, particularly merit description.

Mepacrine has much the same selective action on the malarial parasite and the same limitations as quinine and can be used as an alternative to the latter.

Pamaquin, on the other hand, differs from both quinine and mepacrine in these two respects, and can never be used as a substitute for them, rather is it complementary in its action to these two drugs.

Sulphonamide drugs. Reports on the action of drugs of the sulphanilamide series in the treatment of malaria are conflicting, and research on their potentialities continues.

Paludex is a proprietary oxyquinoline preparation of Belgian manufacture. J. C. Niven carried out exhaustive trials on subtertian malaria with this drug and concluded that it was an inefficient remedy.

Mepacrine.—This drug belongs to the cridine series. It was first synthesized by German chemists and marketed by Messrs. Bayer under the name of *Atebrin*. The drug and drugs closely allied to it have since been manufactured in a number of countries. Mepacrine is the British equivalent of atebrin, but in the U.S.A. the original name is still employed. *Quinacrine*, *Acriquine*, *Haffkinine* and *Crinodora* are the names used in other countries for similar preparations.

Mepacrine is available in two forms :—

(*a*) *Mepacrine hydrochloride* (atebrin hydrochloride of Bayer), a yellow powder sparingly soluble in water. It is generally marketed as a tablet containing 0·1 g. of the drug.

(*b*) *Mepacrine methane-sulphonate* (Atebrin musonate of Bayer) is a soluble preparation for injection. It also is a yellow powder and is put up in ampoules containing 0·375 g. mepacrine methane-sulphonate which amount is equivalent to 0·3 g. mepacrine hydrochloride. It is suitable for intramuscular injection.

Action of Mepacrine.—Mepacrine has an active *schizonticidal* action on all varieties of the malarial parasite and is therefore useful in the treatment of the acute malarial attack (*see* Fig. 46A–E).

It has a poor *gametocidal* action, especially on the crescents of

subtertian malaria. It has also little effect in reducing the relapse rate, especially of benign tertian malaria. The selective action of mepacrine and quinine on the malarial parasite will thus be seen to be almost identical.

Mepacrine has certain *advantages* over quinine, namely :—

1. It is not unpleasant to take and has not the bitter taste of quinine (an important consideration with soldiers).
2. It is effective in tablet form which renders its administration easy.
3. Only a small minority of patients suffer from such minor side-effects as gastro-intestinal irritation, slight headache, depression, etc. These are less pronounced than the tinnitus, deafness, nausea, etc., often associated with quinine.
4. Those with an idiosyncrasy to quinine can take mepacrine with impunity. Mepacrine appears to provoke no similar condition.
5. The onset or threatened onset of blackwater fever is no contra-indication to mepacrine treatment.
6. Mepacrine is excreted from the body more slowly than quinine; it therefore retains its therapeutic action for a longer time after cessation of treatment. This is of special application in malaria prophylaxis.

Mepacrine has certain *disadvantages*, viz. :—

1. Mepacrine, given by mouth, appears to exert its action on the initial pyrexia of the malarial attack somewhat more slowly than quinine. For this reason some authorities advise a preliminary two days' course of a quinine mixture before commencing the routine mepacrine course (*see* Fig. 46C).
2. Some individuals, during or shortly after a course of mepacrine, develop a yellow discoloration of the skin, due to the excretion of the dye into the dermis and *not* due to jaundice. This discoloration may persist for many weeks (up to sixty-nine days).
3. A rare complication, usually occurring at the end of a course of mepacrine, is a transitory psychosis of the acute confusional (toxic) type, which rapidly disappears after cessation of treatment.

Methods of Administration and Dosage.—Mepacrine hydrochloride may be given by mouth in tablet form (one tablet, 0·1 g., *ter die* for six to eight days). It is suitable for the routine treatment of all forms of malaria.

In giving Mepacrine for injection (Mepacrine methane-sulphonate), a dose of 0·375 g., contained in one phial, is dissolved in 2–4 c.cm. of doubly distilled water and injected with the usual aseptic precautions deep into the muscles of the buttock.

One to three injections at intervals of twenty-four hours are usually sufficient, the full course being completed by the oral route.

Absorption of the drug into the blood stream following an intramuscular injection is extremely rapid and intravenous injection is not recommended.

The indications for intramuscular mepacrine are the same as for intramuscular quinine (*see* Fig. 46D).

It is an open question whether intramuscular mepacrine can replace intravenous quinine in the urgent treatment of cerebral and algid malaria. Until more data are available it is probably safer to use intravenous quinine for these grave medical emergencies.

Pamaquin.—This is a quinoline derivative first synthesized by the same group of German chemists. It was originally marketed by Messrs. Bayer and sold under the name *Plasmoquine*. The drug is manufactured in this country under the name of Pamaquin, but in U.S.A. the name *Plasmoquine* has been retained. The French equivalent is *Præquine*.

Its effect on the malarial parasite is, in many respects, complementary to that of quinine and mepacrine ; it can, therefore, *never replace* these drugs, but may be employed, usefully, to supplement their action.

Action of Pamaquin.—Pamaquin is a poor schizonticide and has therefore little action on the acute malarial attack, and should never be used alone (or even in combination) in the treatment of such an attack. It has a marked *gametocidal* action, especially on the crescents of subtertian malaria. These break up and disappear after a very few doses of the drug, whereas their numbers are little if at all affected by quinine or mepacrine.

Most important of all from the therapeutic standpoint, pamaquin has a marked effect on the relapse rate, especially of benign tertian malaria.

Toxic Effects of Pamaquin.—Unfortunately, pamaquin is a toxic drug. The margin between the toxic and therapeutic doses is small, and it should therefore never be given except in minimal dosage and under medical supervision in hospital.

It is suitable only for oral administration.

The chief toxic manifestations are :—

1. Epigastric pain of a dull aching character and of obscure causation.
2. Cyanosis, unaccompanied by dyspnœa or cardiac distress and due to methæmoglobinæmia.

The above symptoms, alone or in combination, occur in a proportion of susceptible individuals even when on minimal dosage ; they usually disappear after withholding the drug for a few days and do not, in most cases, recur if the pamaquin be now readministered. These symptoms occur, most commonly on the sixth to ninth day of administration ; therefore, pamaquin is usually given in a three to five-day course.

Other much rarer toxic manifestations are hæmoglobinuria, resembling blackwater fever, hæmolytic jaundice, and acute yellow atrophy, leading in rare instances to death.

Indications for Treatment.—Pamaquin should be given *not* during the acute attack of malaria, but at the termination of a short course of quinine or mepacrine, when the fever has been brought under control and gametocytes are to be expected in the peripheral blood.

Dosage : Pamaquin, tablets, each 0·01 g. One tablet *ter die* for three to five days.

Suggested combined quinine, mepacrine and pamaquin course :—

1. Quinine gr. 10 t.d.s., or mepacrine one tablet (0·1 g.) t.d.s., till the temperature is normal.

(*Continued on page* 173.)

Explanation of Figs. 46 A—F in pages 167—172..

During the malaria "rush" season there may be little time or opportunity for the preparation or keeping up to date of elaborate case records of individual cases of malaria. Much valuable information may thus be lost.

Under these circumstances many important details, both clinical and pathological, may be incorporated in the individual temperature charts, which are collected when the case leaves hospital and stored for future reference and study at the end of the malaria season when records have to be written and the value of the various treatments assessed.

Information dealing with the following points (amongst others) may be recorded on the chart day by day, symbols being used wherever possible :—

(*a*) Result of daily examination of blood films (thick). (Symbols used :—M.P.=malarial parasites in peripheral blood; G=gametocytes ; C=crescents.)

(*b*) Condition of spleen day by day. (Symbols used :—T=tender but not palpable spleen ; B.P.=barely palpable spleen ; P.=palpable spleen ; P.1=one-finger spleen ; P.2=two-finger spleen, etc.)

(*c*) Any outstanding symptom with date of onset :—*i.e.* epistaxis ; coma ; malarial dysentery, etc.

(*d*) Any specific treatment employed and method of administration if other than oral (*i.e.*—I.M.=intramuscular ; I.V.=intravenous). In many cases, when dealing with potent drugs, it is advisable to add the daily dosage of the drug employed ; also the *total dosage* to date.

If standardized and routine treatments are used they may be indicated at the top of the chart. In these examples :—

A=Standard course of atebrin (mepacrine).

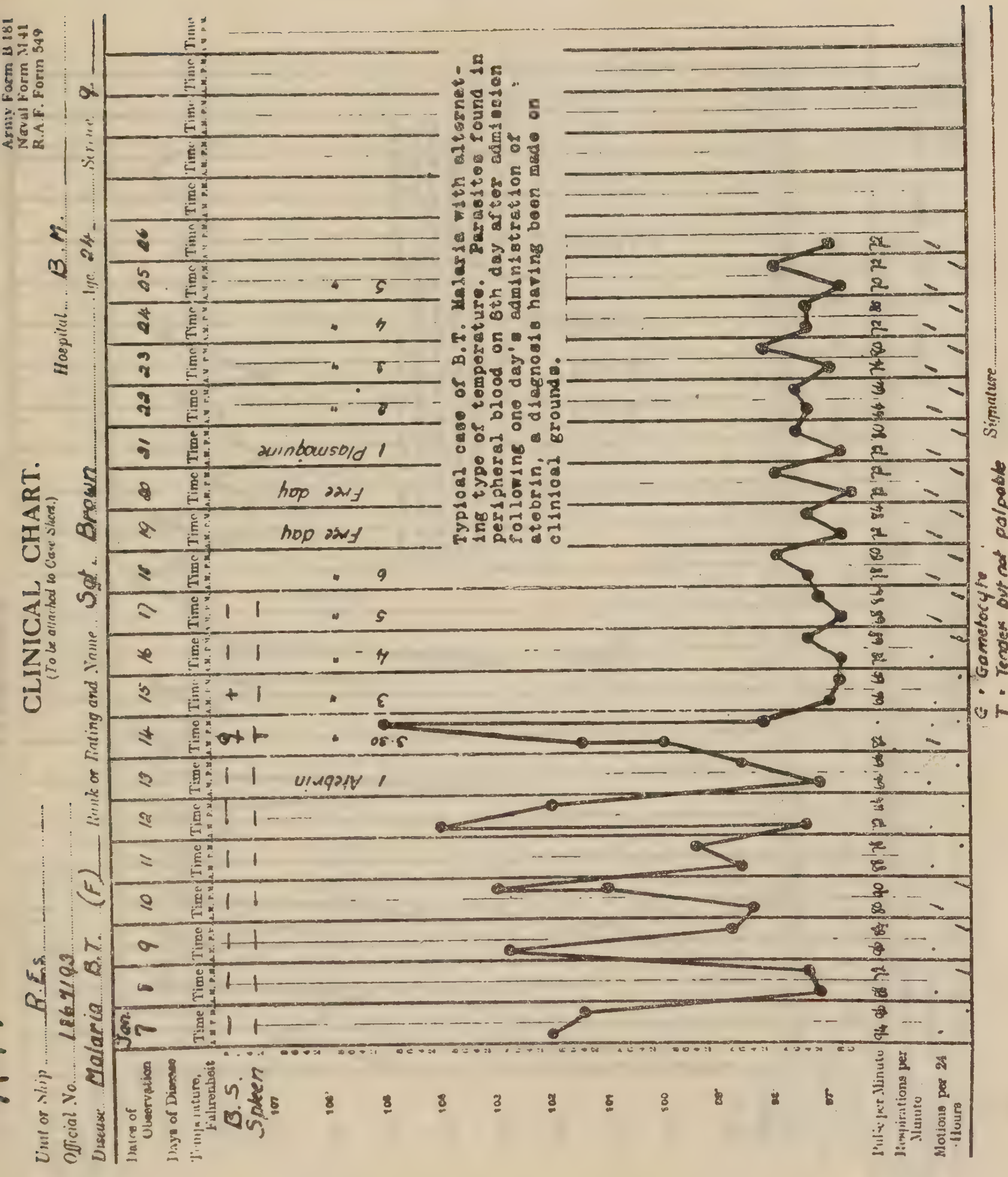
A+P=Atebrin (mepacrine) followed by plasmoquine (pamaquin) in standard dosage.

A.P.=Atebrin and plasmoquine given together in combined dosage.

Q=Quinine ; T=Tebetren, etc., etc.

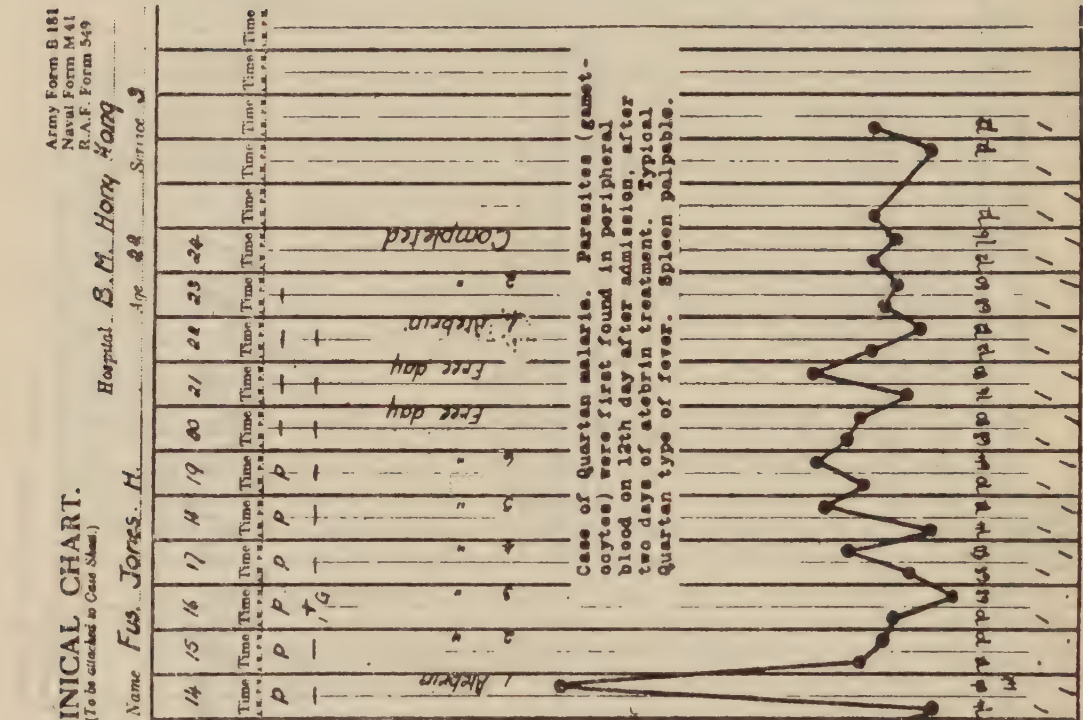
Concise and systematized records such as these, especially if used in conjunction with the Malaria Register (which records such details as the date of onset ; when and where infected ; date and number of previous attacks, etc., etc.), will prove of great value when consolidated records have to be written up.

Fig. 46A.



Case of B.T. (benign tertian) malaria treated with atebrin (mepacrine) 0·1 g. t.d.s. for 6 days, followed after two days' rest, by plasmoquine (pamaquin) 0.01 g. b.d. for 5 days.

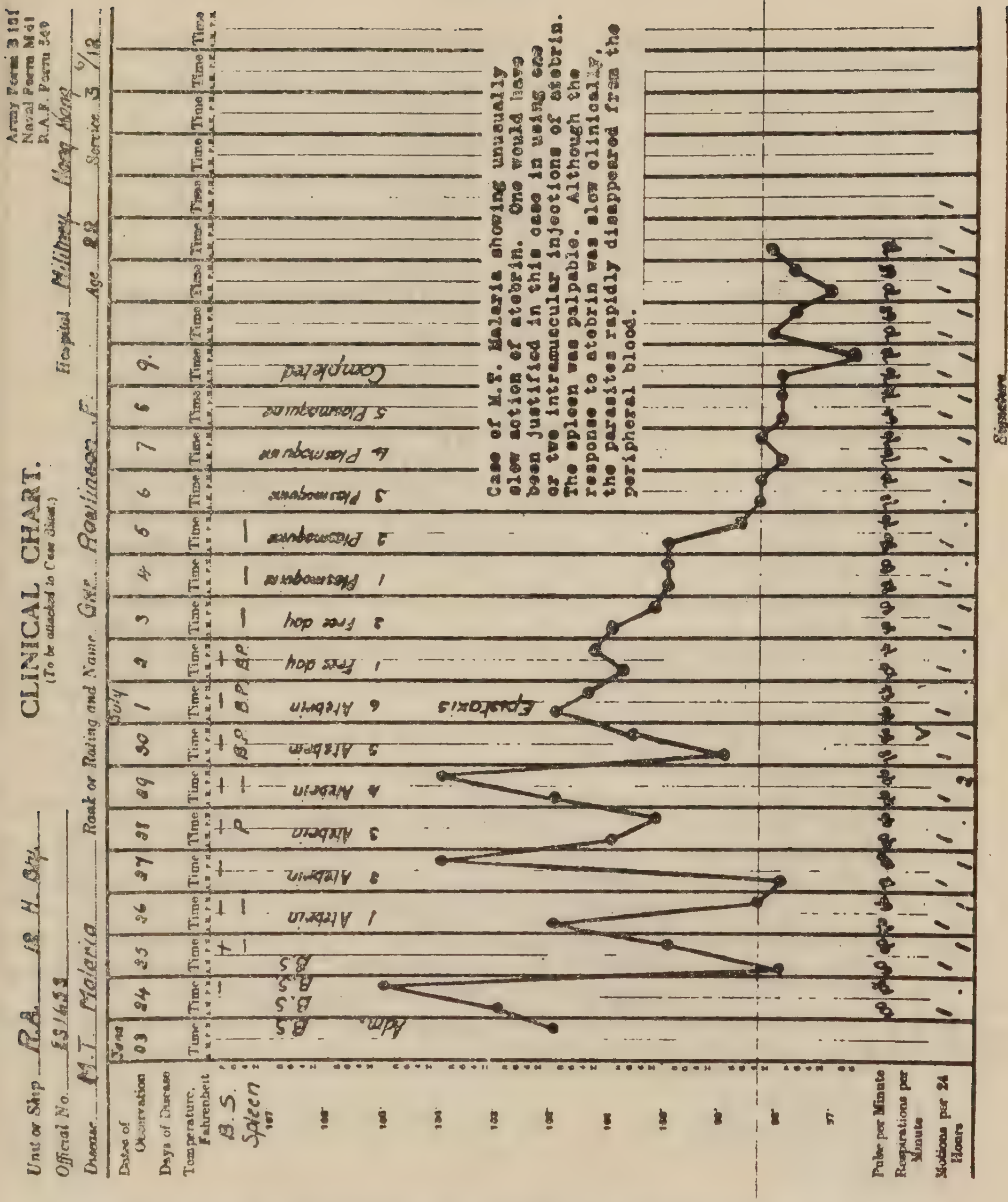
Fig 46B.



Case of quartan malaria treated with an eight-day course of atebrin (0·1 g. t.d.s.), with a rest period of two days after the sixth dose.

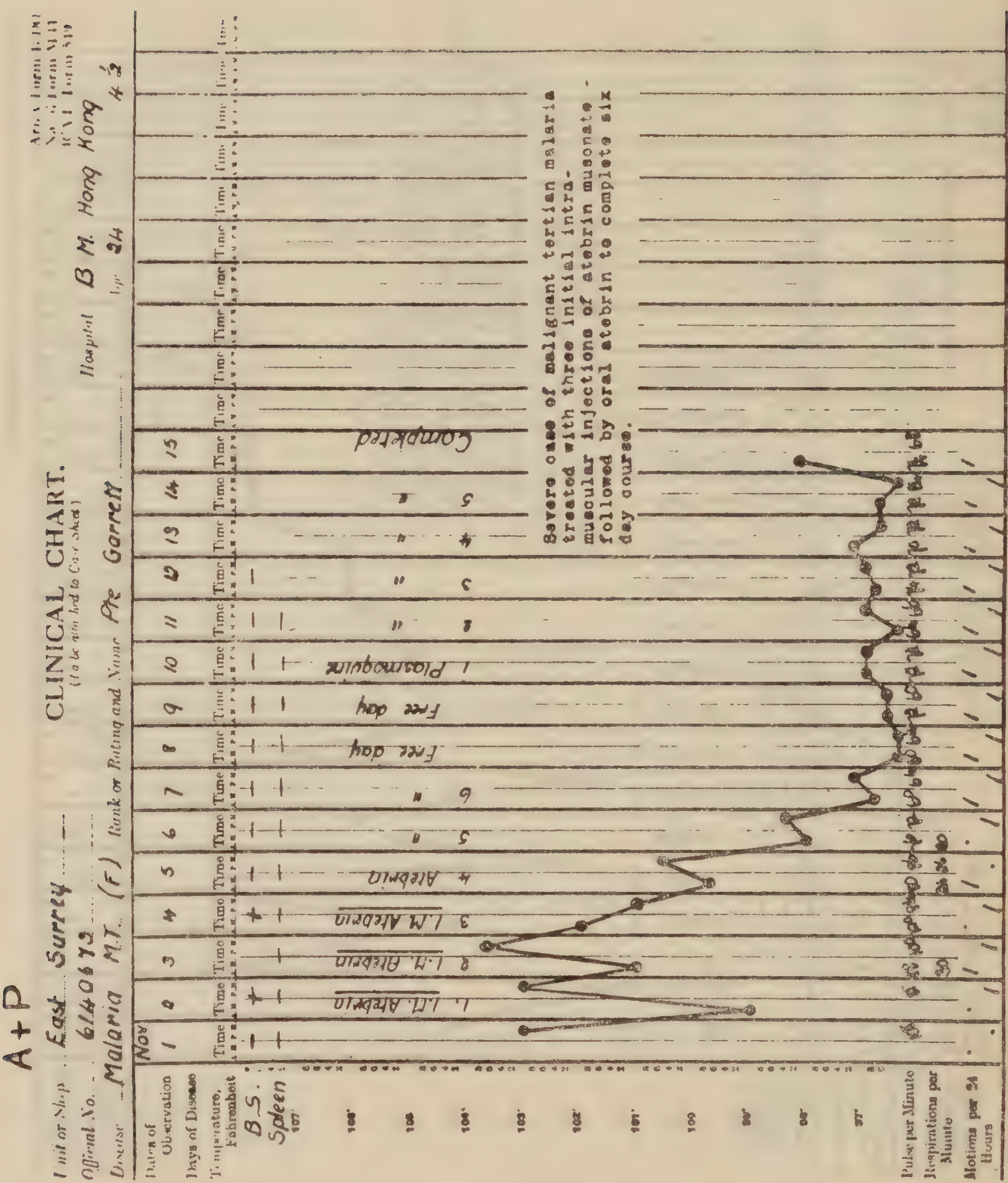
This treatment is effective as far as the individual attack of malaria is concerned, but the omission of pamaquin entails a high relapse rate.

Fig. 46C.



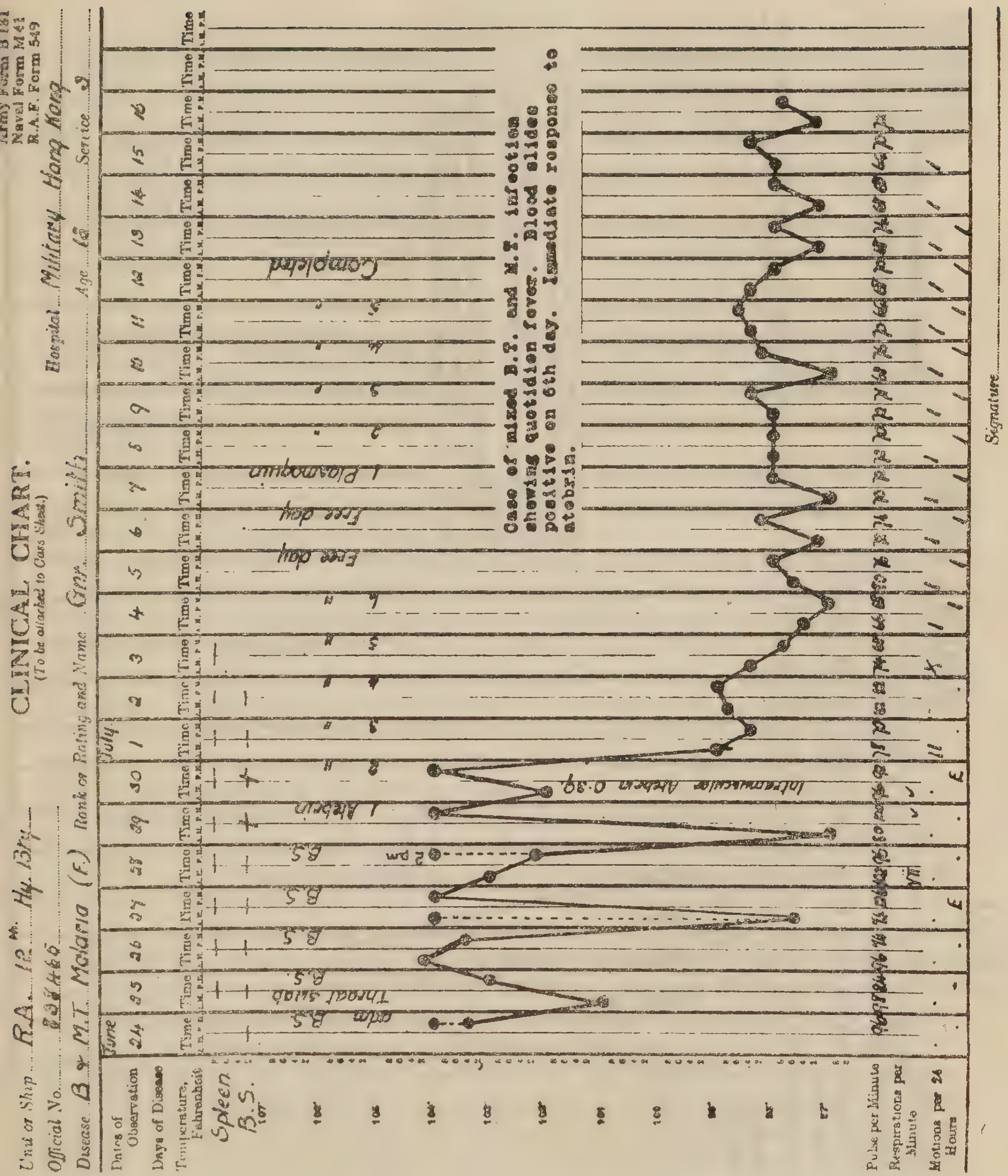
M.T. malaria. Slow response to oral atebrin. A few initial doses of a quinine mixture or of intramuscular atebrin would, in all probability, have produced a more rapid result.

Fig. 46D.



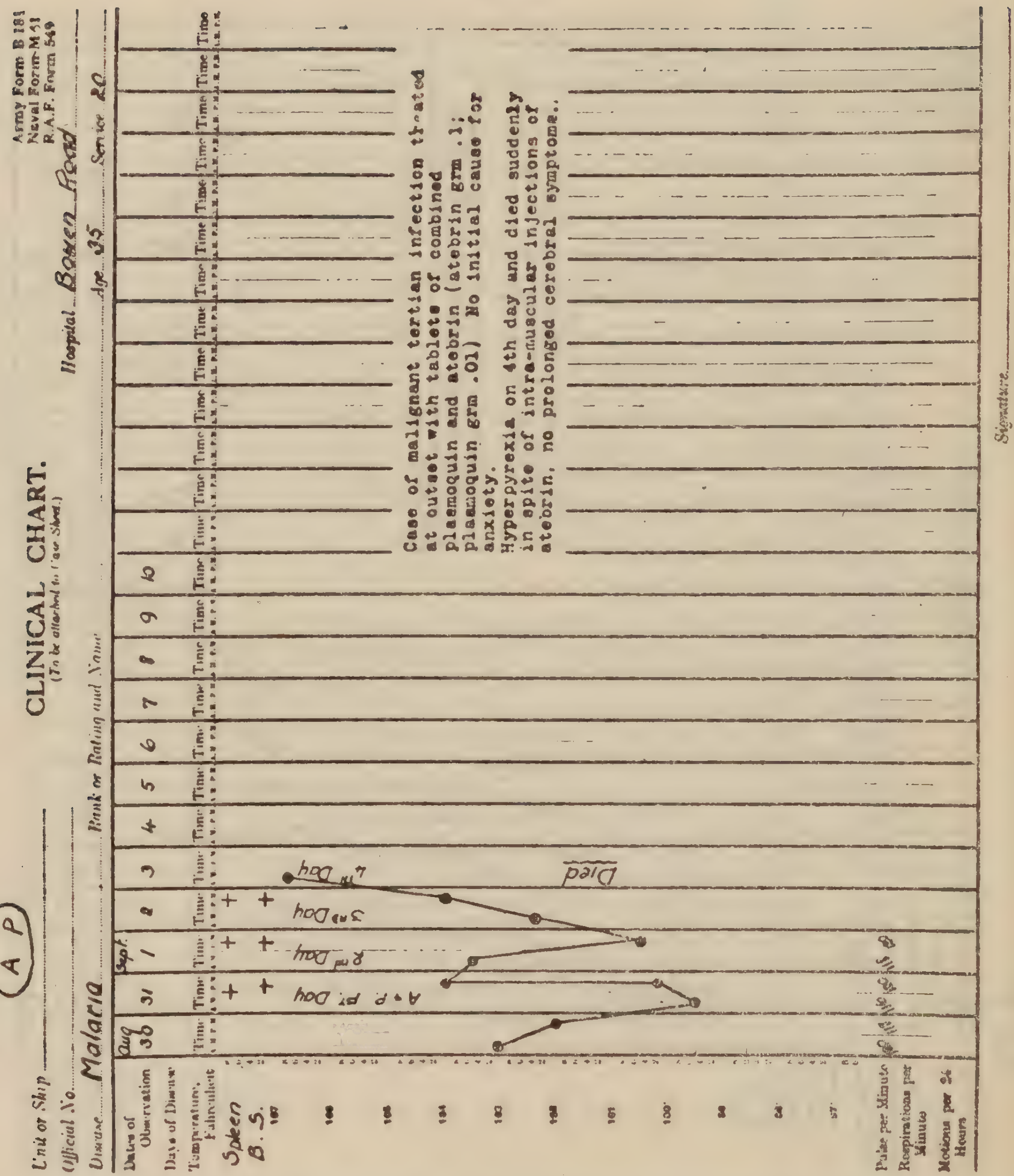
Severe M.T. malaria treated by three initial intramuscular injections of atebrin at daily intervals, followed by oral quinine to complete the six-day course; this being followed after a rest period of two days by a five-day course of plasmoquine (0·01 g. b.d.).

Fig. 46E.



Case of mixed M.T. and B.T. infection. Rapid response to atebrin ; first dose by intramuscular injection.

Fig. 46F.



Case of M.T. malaria who died suddenly whilst under treatment with tablets containing atebrin and plasmoquine in combination.

2. Mepacrine one tablet t.d.s., or quinine gr. 10 t.d.s., for seven days.
3. Two days' freedom from drugs.
4. Pamaquin, 1 tablet (0·01 g.) t.d.s. for three to five days.

Note.—Mepacrine and pamaquin should *never* be given together, *i.e. concurrently*, either in one pill (a combined pill is marketed called Atape) or in separate doses. They should always be given *consecutively* ; mepacrine first, preferably followed by two days' rest ; then pamaquin.

The toxic effects of both drugs appear to be enhanced by their administration together (*see* Fig. 46F).

This objection does not operate in the case of combined quinine and pamaquin.

General Treatment.—The diet should be fluid until the paroxysm has subsided. Plenty of fluid should be given to combat dehydration due to excessive sweating. If dehydration is extreme a rectal or intravenous saline may be necessary and should not be delayed until it is too late.

If there is hyperpyrexia, *i.e.* a temperature of 105° F. or over, the patient must be tepid-sponged and, if necessary, douched or bathed as for heat-stroke (*see* p. 122).

In severe cases with marked jaundice, as in the form of malaria known as bilious remittent fever, plenty of sugar should be given in the form of sweetened drinks, or as glucose by the bowel or by intravenous injection in a 5–10 per cent. solution. Vomiting, which may be severe and obstinate, may tax all our therapeutic resources. Adrenaline hydrochloride, 20 minims of a 1/1,000 solution in half an ounce of water, given hourly until the vomiting stops, is often an effective remedy. Sips of iced champagne may act like a charm, especially in nervous women.

Severe headache may be treated with aspirin, Veganin, or A.P.C. (aspirin, phenacetin and caffeine) powder, or the two or three fifteens mixture, and insomnia will usually respond to one or other of the above.

All cases of malaria should be kept in bed during the febrile period of the attack and for two or three days after the temperature has returned to normal. Thereafter they may be allowed up but should remain in hospital until the course is completed, usually about a fortnight in an uncomplicated attack.

If the military situation allows it the patient may be discharged to a week's excused duty at the end of his hospital course, during which time he reports daily at his medical inspection room.

A blood picture should be taken at the end of his anti-malarial course (or before, if he looks unduly anæmic). Only those with anæmia require iron, which may be given by mouth in massive dosage. A fortnight's course of an adequate iron mixture cures most cases of anæmia due to malaria. The routine administration of iron " tonic " for all those who have completed an anti-malarial course, except possibly as a placebo, is unscientific and probably does little good.

Ascoli's method of treating *malarial splenomegaly* consists in daily intravenous injections of adrenaline. Commencing with an initial dose of 0·01 mg., the dose is increased daily until a daily dose of 0·1 mg. is reached and is maintained at this level for twenty days; a total of about 30 injections is given. Immediately following the injection the patient usually complains of pallor and trembling which is followed by a rapid diminution in the size of the spleen. (1·0 c.cm. of adrenaline 1/1000 solution contains 0·01 mg.)

Some authorities follow up the adrenaline with quinine on the assumption that the parasites, forced to leave the spleen owing to the reduction in size of that organ, find their way to the peripheral circulation where they are effectively attacked by the quinine.

Malaria Relapse.—The treatment of a malarial relapse is the same as that for the primary attack. As a general rule the relapse is milder, runs more truly to form, and responds more rapidly to malarial therapy than does the primary attack.

As mentioned above, long "follow" courses of quinine are not now given—except in small dosage as a clinical prophylactic—in the hope of preventing relapses; each relapse is now treated as it occurs.

PROPHYLAXIS

Mosquito prevention has already been dealt with in detail in the section on Arthropod Pests. The siting of camps as far from infected localities such as native villages, "paddy" fields, low-lying marshy ground, etc., as is consistent with the strategic requirements of the situation, is a matter of considerable importance and must not be overlooked.

A valuable general prophylactic measure is the search for and treatment of chronic malaria (gametocyte) carriers in the endemic zone as far as this is possible.

The important measure which remains to be considered is chemo-prophylaxis.

No true *causal* prophylactic against the parasite in its early infective stage as injected by the mosquito (sporozoite) has yet been found. Pamaquin has been claimed to be a causal prophylactic, but in doses too large for therapeutic safety.

Quinine, whilst not a true *causal* prophylactic is a useful *clinical* prophylactic and, in small daily doses (gr. 6 daily) will keep a considerable proportion of those *whilst taking it* free from clinical attack, even in a highly malarious district. That this protection is, however, only very partial is shown by the Macedonian campaign when many thousands suffered from repeated attacks of virulent malaria although they were on prophylactic quinine.

Soon after the cessation of this daily prophylactic dose, even if it be taken continuously and conscientiously for a year or more, a large proportion of those who have been infected with sporozoites will suffer a clinical attack, often it is said of unusual severity, of malaria. It is therefore considered that the term "suppressive" should replace the word "prophylactic" as being a more accurate description of its action.

Suppressive quinine has largely gained its reputation as a means of individual protection against malaria in hyperendemic foci of the disease, particularly in those districts where blackwater fever is common.

In certain hyperendemic foci (*i.e.* tropical Africa) small daily doses of quinine are taken by almost all Europeans. Under these circumstances it is usually advisable that the daily dose of quinine be continued for some time after leaving the endemic area.

As regards its employment with troops in the field, it is definitely indicated with a large force in a highly malarious country with large numbers of mosquito vectors, especially where the troops are only temporarily exposed. It is also indicated in the case of small parties or detachments billeted temporarily in such areas.

Suppressive quinine is not recommended in the case of a force operating in a moderately malarious district with no special abundance of mosquito vectors. It is better in such cases to allow the odd case of malaria to occur and to treat it as it occurs. The same remarks apply to mepacrine prophylaxis.

Mepacrine, whilst also only a *clinical* prophylactic, is slightly more effective than quinine, and, being excreted more slowly, its effects last considerably longer after cessation of treatment. It has the added advantage of being given twice weekly, preferably on two successive days. It is best given as two tablets (0·2 g.) bi-weekly. This dose may be increased during active operations.

Whichever drug is used certain general precautions must be observed. The men should be paraded under an officer with the medical officer in attendance. Care must be taken that every man receives and *swallows* his dose and that there are no shirkers.

Abstracted from Fourth General Report of the Malaria Commission, League of Nations, on the Treatment of Malaria. (*Published, December,* 1937.)

It is noted that quinine hydrochloride in a daily dosage of 1–2 g. for five to six days usually suffices to cause trophozoites to disappear from the peripheral blood (*i.e.* to cure the acute attack), and not to make their reappearance until after a latent period of varying length, constituting the first relapse.

Whilst quinine, in the dosage mentioned, has a parasiticidal action on all the gametocyte stages of *P. vivax* and *P. malariæ*, it has only a very slight action on the crescents of *P. falciparum.*

Whilst quinine has a clearly marked effect on the frequency of relapses, primary *P. vivax* and *P. malariæ* infections may be followed by a relapse rate as high as 50 per cent.

Quinine treatment with the usual doses does not affect the patient's general health if the period of administration is limited to the strictly limited number of days (*i.e.* five to seven days). In such a case there is no good reason for thinking that this treatment hinders the process of immunization, but ill-effects may occur when treatment is unnecessarily prolonged.

Mepacrine in daily doses of 0·3 g. for five to seven days acts in

the same way as quinine given for the same period. There is no reason why either mepacrine or quinine should be preferred.

Pamaquin.—Treatment with quinine or mepacrine may usefully be followed by pamaquin treatment in order to diminish the number of gametocytes and the risk of relapses. The association of quinine with pamaquin represents one of the most efficacious methods of treating benign tertian and quartan malaria. Treatment by average doses of quinine and pamaquin (even only 0·02–0·03 g. pamaquin twice a week) greatly reduces the number of relapses of benign tertian malaria and, in some areas, of malignant malaria.

The *simultaneous* administration of mepacrine and pamaquin appears to aggravate the toxicity of each. *Consecutive* treatment, first with mepacrine (0·3 g. daily for five to seven days) followed by pamaquin (0·02 g. daily for five days) diminishes substantially the number of relapses both in malignant tertian and, more especially, in benign tertian and quartan malaria.

MYIASIS

This condition, the presence of parasitic dipterous larvæ in the body, is usually classified, according to the site of the lesions, into cutaneous, nasal, intestinal, etc., varieties. Patton's division, based on the breeding habits of the diptera concerned, is much more satisfactory. He recognizes three groups of Myiasis-producing flies—Specific, Semi-specific, and Accidental.

1. *Specific*, where the larvæ can develop in living tissues only. Examples of this group are: *Chrysomyia bezziana*—the commonest cause of human myiasis in India; *Cordylobia anthropophaga*, the well-known Tumbu fly of Africa (see Plate 8 and below); and the Œstridæ, Bot or Warble flies.

2. *Semi-specific*, those flies which breed normally in decomposing matter, but which may occasionally attack living tissues, being attracted by foul discharges, blood, etc. Amongst such flies are *Chrysomyia megacephala* (=*dux*), the common Indian bazaar fly; *C. macellaria*, the American screw-worm fly; several species of *Lucilia* and certain *Sarcophaga*.

3. *Accidental.*—This group includes those flies whose eggs or larvæ are swallowed, usually in food or drink, and develop in the intestine, this occurrence being accidental and no part of the fly's ordinary development. Blow flies; species of *Sarcophaga*; some Anthomyidæ, especially *Fannia canicularis*, have been found, amongst others, and one of the Aschiza, *Apiochæta xanthina*, may not only pupate in the intestine, but the adults may even hatch out in this site.

Most of the larvæ causing dermal myiasis do not pierce the skin, but invade wounds, or sores, however small. Some attack the mouth, nose, eyes, ears, or genital orifices, and unless the nature of the trouble is recognized and vigorous treatment applied, there may be great destruction of tissues and even death. Consequently all

septic wounds or sores should be effectively protected against flies, particularly in the case of children and helpless people, and those with offensive discharges from the nose or ears should keep the orifice plugged with an antiseptic dressing.

Diagnosis.—The diagnosis of myiasis is established by discovery of the larvæ concerned. As there is still much to be learned about myiasis, no effort should be spared to identify the species of fly responsible for the lesions. Kill a few of the mature larvæ by dropping them into "bubbling" water (*i.e.* 80° C., just short of boiling water) and preserve them in 80 per cent. spirit. The remainder of the larvæ should be allowed to complete their development, as this will facilitate identification. The larvæ of specific myiasis-producing flies, like *C. bezziana*, will not develop in dead flesh, but should be placed in a wound on the body of a living animal. The larvæ of semi-specific myiasis producers will develop in meat, but this must be carefully protected from contamination by the eggs or larvæ of other flies. Flies may show most uncanny ingenuity in providing for their offspring by dropping eggs, or larvæ, through tiny openings, or depositing them in the neighbourhood of small apertures through which access may be had to meat, etc. Patton has found that the only certain method of excluding contaminating larvæ is to make a secure parcel of the required meat in several sheets of paper. If this becomes damp, further sheets are employed, otherwise foreign larvæ may pierce the softened-paper. The larvæ will pupate in the folds of the paper and the pupæ should then be removed and two or three placed in each of a number of tubes. When the adults emerge they should be kept for a day or two to allow them to harden, and then killed and pinned. For the identification of the various stages of flies concerned in myiasis in India, Patton's invaluable papers on "Indian Calliphorinæ," in the *Indian Journal of Medical Research*, 1920–22, should be consulted, and the diagnosis confirmed by an expert.

Treatment.—Remove the larvæ by douching with chloroform water. Local application of liquid paraffin materially assists extraction. In rhinal myiasis it may be necessary to open the frontal or other sinuses in order to irrigate efficiently. After removal of the larvæ, treat the residual inflammation on ordinary lines.

Cordylobia anthropophaga (Plate 8)

The form of dermal myiasis due to *Cordylobia anthropophaga*, or an allied species, is of sufficient importance from a military standpoint to require a separate note. In parts of the African campaigns of the Great War this condition was common, and proved troublesome and crippling, especially to the Indian troops.

The fly lays its eggs, as many as 300 at a time, on the ground, dry sand previously contaminated with excreta being favoured. The resulting small larvæ may remain alive for ten days or even longer without food, and are not readily seen unless disturbed. When opportunity offers, the larvæ creep from the sand, soil, etc., on to their hosts. By means of the buccal spine the tiny larvæ penetrate

the skin, the actual passage through the epidermis causing little disturbance. When mature they drop out, burrow in the ground and pupate. It is possible that the fly may lay its eggs on clothing, and, moreover, underclothing, bedding, etc., often transmit infection from the ground. Larvæ placed on cloth may remain alive for at any rate nine days. Infection of the domestic dog is commonly observed, but the most important host appears to be the rat.

Symptoms.—The lesion produced is like a small boil or urticarial weal, in the centre of which there is an opening which may be obscured by discharge or may be patent, when it looks black in colour, owing to the presence of excrement from the posterior end of the larva which may be visible. Pressure on it causes pain. Around the hole the skin is inflamed and very itchy. In East Africa the commonest site appeared to be the forearm, but it is stated that in Europeans the scrotum, upper part of the thighs and buttocks are most frequently attacked, and it has been suggested that infection takes place when persons are using the latrine. The larvæ may be found in any exposed part, and multiple infections occur. When small they are easily squeezed out, but if neglected attain maturity and may be associated with a little suppuration.

Treatment.—Extract the larva with forceps. This process is less painful if a little chloroform is injected into the larva before its removal. Simple expression is often effective, and is facilitated by free local application of liquid paraffin. Allay the local irritation. Paint the skin with iodine in potassium iodide after extraction.

ORIENTAL SORE

This condition is better termed Cutaneous Leishmaniasis, for the lesion is not confined to Oriental regions nor is it always an open sore. It is commonly known as Bagdad Button and Aleppo Sore.

The causal organism is the protozoon *Leishmania tropica*, infection with which is almost certainly acquired through the agency of *Phlebotomus*. Sergent and others have caused oriental sore in a locality where the condition is unknown, by rubbing into the excoriated skin a saline extract of crushed *P. papatasii* sent from an endemic area.

It is possible that the disease may be acquired by personal contact with an affected case, and it is worth noting that the condition occurs in dogs. Experiments have shown that, under certain conditions, house flies can act as mechanical vectors of *L. tropica*, and it is possible they may sometimes infect open sores and wounds.

A distinction must be made between oriental sore and post-kala-azar dermal leishmaniasis, a condition which occasionally follows successful treatment of the latter disease.

Symptoms.—The incubation period appears to vary from a fortnight to a year. The lesion may appear on any exposed part of the body, but is most common upon the upper extremities, especially the forearm and hand, and on the face, especially the ear and nose,

in short, those exposed parts of the body most vulnerable to the bites of the infecting *Phlebotomus*. It is often multiple, being auto-inoculable. It commences as a small red papule covered by a tiny reddish brown scale, and indeed suggests what might be called an indolent mosquito bite. It is less irritating than the latter and may cause no local discomfort. The papule, at first shotty to the feel, gradually enlarges, becoming purplish in colour, softer in consistence, glazed on the surface, more markedly scaled, and is surrounded by a narrow area of chronic inflammation.

After a varying period, usually three or four months, ulceration may occur, frequently as a result of an injury (Plate 23). The ulcer is painless and may be an inch or more in diameter. The ulceration is superficial, the whole affected area being somewhat raised and surrounded by a hard red edge in which active multiplication of the parasites takes place and in which they are most readily found, especially if puncture by a needle or a fine glass pipette is employed. The ulcer exudes a yellowish secretion, is often foul smelling, and becomes covered by a tough, adherent, dark scab. If the edges of this scab are forced up the yellow pus wells out. This pus formation is probably due to secondary bacterial invasion. This may also lead to an enlargement of neighbouring lymphatic glands. Under the scab the ulceration spreads and the surrounding tissue may become œdematous.

Occasionally the lymphatic vessels draining an affected area are invaded by the parasites with the formation of nodular swellings which may break down and ulcerate.

Healing sets in after six or twelve months, the unhealthy yellowish granulations being replaced under the scab by healthy pink ones and the ulcer becoming shallower. Eventually a white or pink scar is left which may be very slightly depressed and is disfiguring.

One attack confers immunity. There are no constitutional symptoms.

Various other clinical varieties may be encountered. In the keloid form the organism causes raised, shiny, softish, movable mounds of tissue covered by pinkish skin. These do not ulcerate, but resolve by a gradual shrinkage and drying. Or large heaped-up papillomatous masses may result, which may resolve, as in the keloid form, or break down and give rise to open sores. The name espundia is given to a variety of cutaneous leishmaniasis found in South America in which destruction of mucous membranes and cartilage takes place, and it differs further in that there is no tendency to spontaneous cure.

Diagnosis.—This can only be made with certainty by the finding or cultivation of the specific parasite. The parasites may be found in pus from the ulcer surface, but are more readily discovered by puncture of the unulcerated margin (Plate 22).

Differential Diagnosis.—Cutaneous leishmaniasis must be distinguished from the so-called trench sores which, like the South African veldt sores, are due to staphylococcal infection. This can only be done with certainty by microscopic or cultural examination, but in trench sores the condition is more acute and less lasting than in the specific infection. Ulcus tropicum must also be distinguished.

This is readily done with the microscope (*see* Skin Diseases), while clinically oriental sore differs in never becoming phagedænic. Rodent ulcer, extra-genital chancre, post-visceral dermal leishmaniasis, etc., are other conditions which may simulate oriental sore.

Treatment.—Intravenous injections of antimony tartrate, or of one of the pentavalent compounds, as described in the section on kala-azar. This is the treatment of choice for multiple sores, or for those causing disfigurement or serious inconvenience. But, unfortunately, lesions on the face, and especially those on the nose, are the most likely to prove resistant to intravenous antimony. Usually from 8 to 15 grains of antimony tartrate will suffice and, as in kala-azar, the pentavalent compounds are more effective. These are given as described in the section on that disease.

Local application of tartarated antimony as an ointment in a strength of 2 per cent. is often successful. Apply twice a day, ceasing the application when a sharp local reaction occurs. This may take about twenty-four hours or more to develop. Subsequent healing is assisted by fomentations and simple dressings. For children, commence with an ointment one-quarter of the strength mentioned.

Injections of emetine distributed around the margin and under the base of the lesion have resulted in cure. Give $\frac{1}{8}$–1 grain at each sitting, leaving an interval of several days between treatments. To force the solution into the tense tissues a syringe with a tightly-fitting needle and piston is essential. Or, $\frac{1}{4}$ grain of berberine sulphate in 1·5 c.cm. of distilled water may be given in the same way. Two such injections are said to suffice.

In India, a mass treatment by scraping the nodules and ulcers under gas, followed by the application of pure carbolic acid and a covering of elastic adhesive has been advocated.

Applications of carbon dioxide snow applied for 5–30 seconds every ten days have also given good results.

In the Punjab injections of 0·5–1·0 c.cm.of a vaccine made from cultures of *L. tropica* have produced many cures, whilst in Russia, prophylactic subcutaneous injections of living cultures into an arm or leg, producing an immunizing sore where it will not cause disfigurement, have been attempted with some success.

The older methods of treatment by scraping or excision, or by application of caustics such as permanganate of potash in fine powder, have their exponents. Some refractory lesions are stated to have been healed by utilizing the patient's immunizing powers and treating the sore with dressings of his own blood serum.

Oriental sores, especially those in an early stage, often yield satisfactorily to various methods of electrical therapy, though some prove refractory. Using X-rays, the most successful dosage is a subintensive one equal to three-quarters of the erythema dose, repeated in about three weeks if necessary. No filter is required, but the recognized precautions in this type of treatment must be observed.

Ionization often proves successful in these cases. Zinc or antimony salts can be applied by means of suitable active electrodes to the area of the sore. Several applications of large currents up

to 30–40 milliamperes according to the size and depth of the sore are beneficial, but it must be remembered that current densities sufficient to be of real value are painful in application (McGrigor).

It will often be found that the case which stubbornly resists all known methods of treatment eventually heals of itself. This tendency to self-limitation should be remembered, otherwise cure may be attributed to whatever treatment chances to coincide with the natural process of resolution.

Prophylaxis.—Paint the site of all fly and other insect bites with iodine as soon as possible. Warn against the danger of infection by personal contact and that of auto-infection by scratching. Sleep under a net of such a mesh that sandflies (*Phlebotomus*) are excluded.

PARATYPHOID FEVER

The paratyphoid fevers are world-wide in their distribution, and prevail wherever defective sanitary conditions favour their spread. Generally speaking, paratyphoid A infections are most common in the East, whilst paratyphoid B is more commonly met with in Europe and temperate climes generally. Paratyphoid C occurs in the Balkans, but a few cases are recorded annually from India.

Etiology.—At least three separate and distinct bacilli are to blame, *i.e. B. paratyphosus* A, *B. paratyphosus* B, and *B. paratyphosus* C. They closely resemble *B. typhosus* in their morphology and general cultural characteristics, but differ from it in the way they behave with specific immune sera and in certain of their cultural reactions. From the pathological standpoint paratyphoid A is more closely related to typhoid than to paratyphoid B. As in typhoid and bacillary dysentery, so in paratyphoid, the methods of infection may briefly and alliteratively be described as careless contacts, carrier cases, chiefly cooks, dirty drinking water, the dust of dried dejecta, and the repulsive regurgitation, dangerous droppings and filthy feet of fæcal-feeding flies fouling food. Some outbreaks of paratyphoid B have been traced to infected meat, but here there is a possible confusion with *B. ærtrycke*.

Thanks to the universal practice of chlorination, water infection does not seem to have bulked largely in the war of 1914–1918.

Symptoms.—*Paratyphoid A and B.*—The average incubation period is probably about ten days. It is not possible to discriminate clinically between paratyphoid A and B, which can be differentiated from one another and from true typhoid only by laboratory tests. The first runs a slightly longer course and seems to be on the whole a milder disease.

The onset may be gradual like that seen in typical typhoid, but in the majority of cases it is comparatively sudden and in some it is exceedingly sharp. Headache and abdominal pain, or rather uneasiness, are the first signs as a rule, and in cases with slow onset

there is general malaise, diarrhœa which may pass off, slight shivering fits, pain in the back and limbs, and sometimes epistaxis. The patient carries on till he is no longer fit for his duties. The opposite class of case is where a patient suddenly develops abdominal pain, which may be severe and colicky in type, diarrhœa and intense headache, feels feverish, shivers, may retch or vomit, and is speedily prostrated.

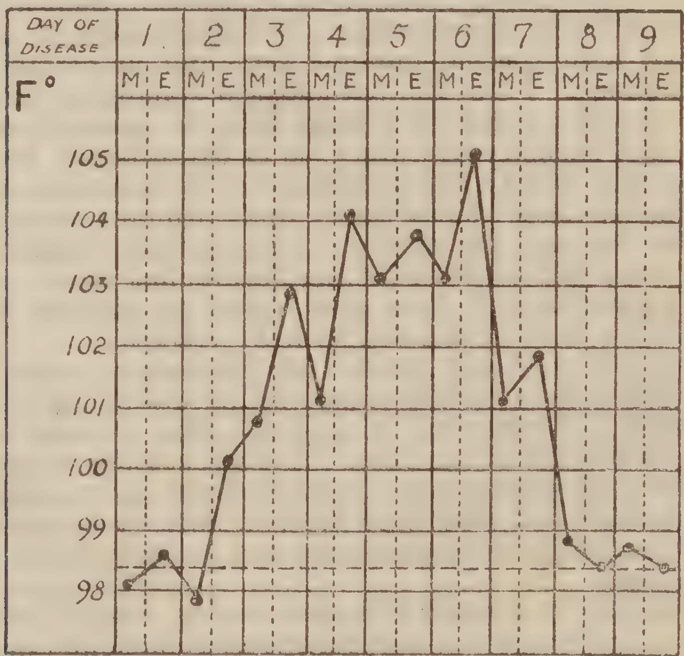
The onset is indeed very like that of influenza, but lacks the catarrhal element, though cough and sore-throat may develop later or may be present from the outset, or an early bronchitis may mask the primary infection. Vertigo and deafness sometimes occur, and a certain proportion of patients are constipated, especially in hot climates. Pain over the region of the gall bladder has been noted in the earlier stages of the fever.

The temperature rises fairly rapidly, but to no great height—somewhere between 100° and 101° F.

There would seem to be very slight cases of the disease where the patient is only really ill for about a week, but a typical paratyphoid B attack runs a course of anything between ten and eighteen days and a characteristic paratyphoid A exhibits a three weeks' pyrexia.

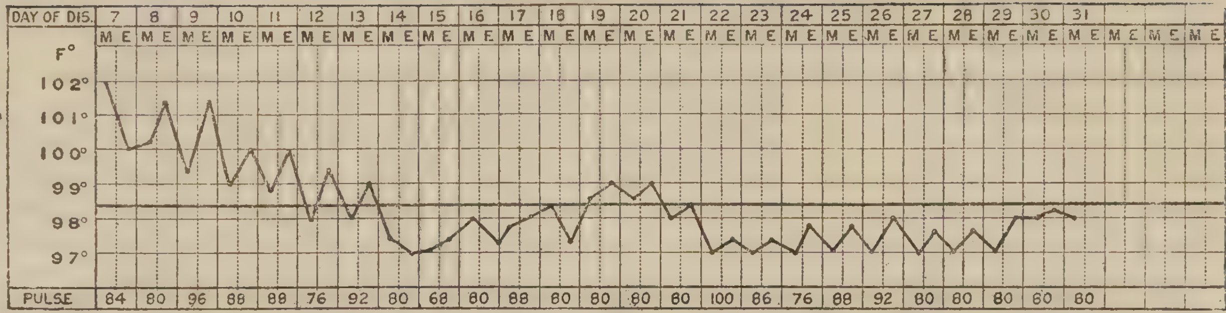
Even at the height of his illness the average paratyphoid case does not look seriously ill. The general temperature course is indicated in the accompanying charts (Figs. 47 to 54), and only a small number of cases exhibit anything approaching a true typhoid state. In all, however, especially in the early stages, there is a certain lethargy or apathy. A flushed face is rare and the eyes are

Fig. 47.



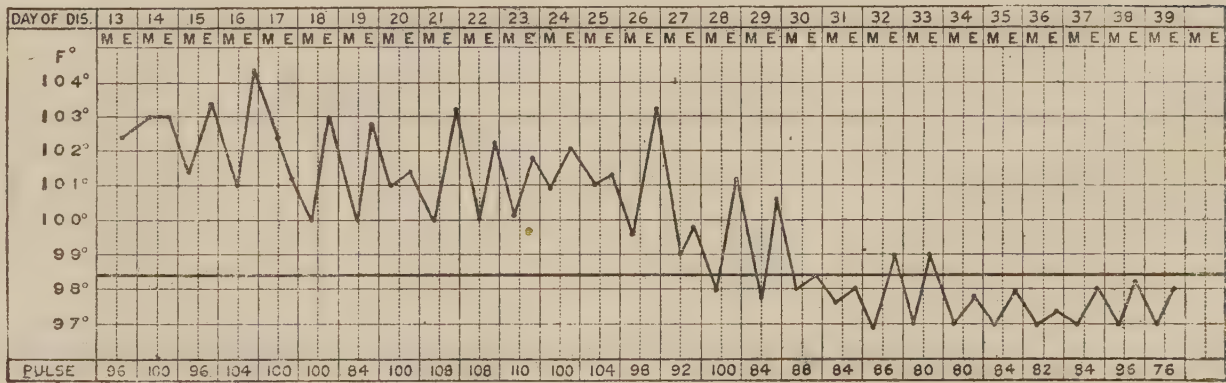
Short attack Paratyphoid. Gradual onset and rapid defervescence.

Fig. 48.



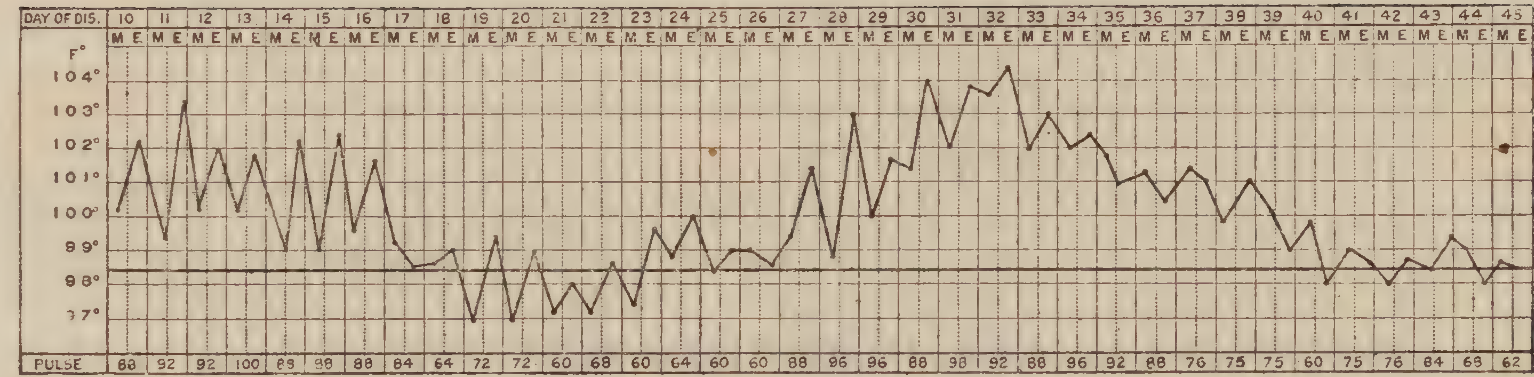
Typical mild short Paratyphoid A. Thirteen days' pyrexia.

Fig. 49.



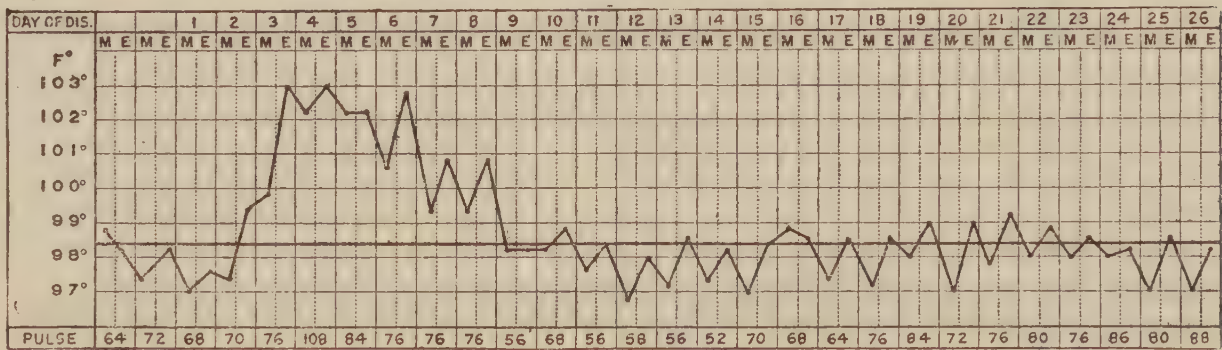
Paratyphoid A, mild but prolonged. Thirty days ever.

Fig. 50.



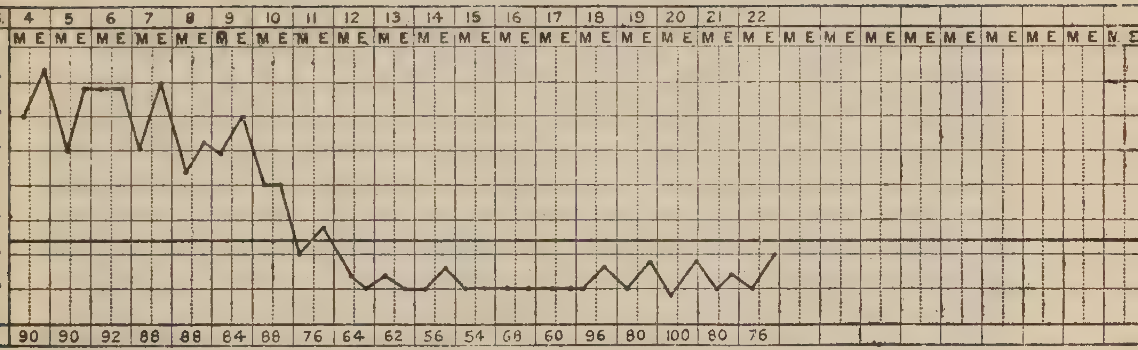
Rather evere Paratyphoid A. Pyrexia of average duration and relapse.

Fig. 51.



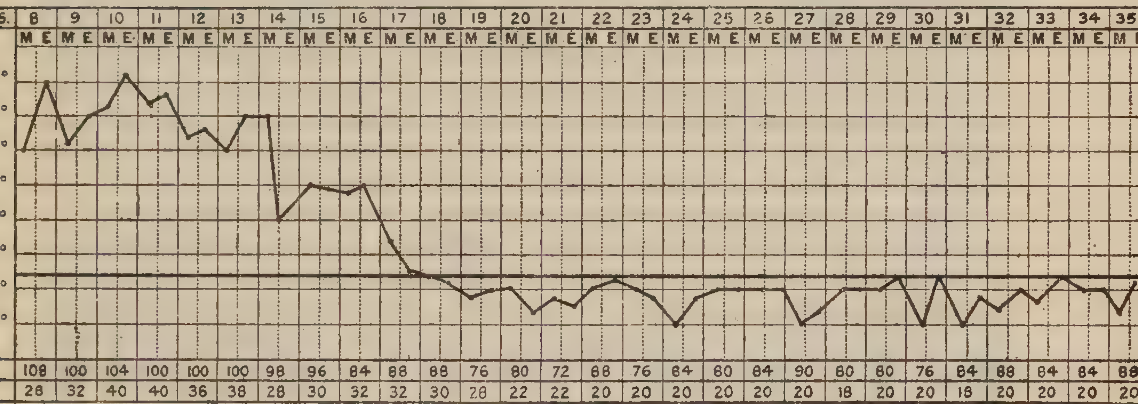
Typical short Paratyphoid B. Rapid rise and quick fall on ninth day.

Fig. 52.



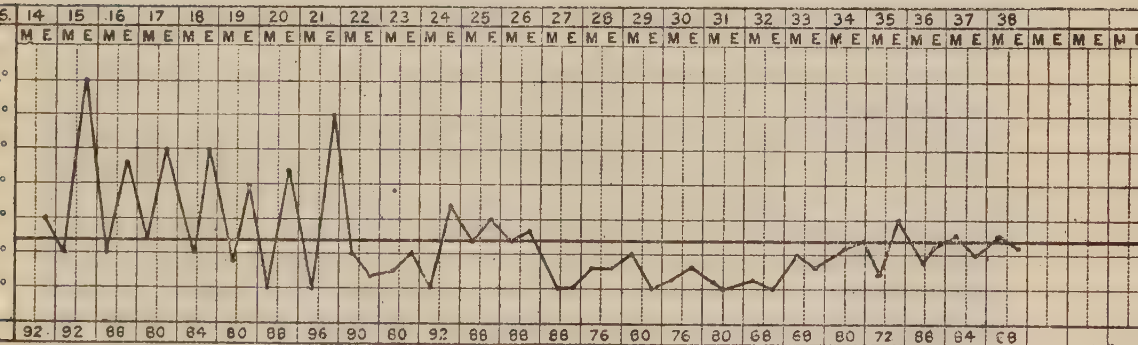
Typical rather severe Paratyphoid B. Eleven days' pyrexia.

Fig 53.



Severe toxic case of Paratyphoid B. Pyrexia of seventeen days.

Fig. 54.



Mild case of Paratyphoid B with intermittent temperature.

dull and often kept about half closed owing to the headache, which is the patient's chief complaint.

The spiky nature of the temperature will be apparent and is very characteristic. It rarely falls to 99° F. and as rarely rises to 103° F. In most cases it keeps swinging between a couple of degrees up at night and down in the morning, but occasionally missing the remission. Now and then one meets with a case showing intermission. In paratyphoid B infections so-called undulant cases have been described and a type with low irregular pyrexia. Of all symptoms the pulse rate is probably the most important for, unless the patient has been smoking, it is nearly always slow and very often slower, as compared with the temperature, than it would be in true typhoid. Thus, a pulse rate of 60 may coexist with a temperature of 100° or 101° F. It varies, however, and several have noted a high rate coinciding with a high temperature. Other notable features are a certain compressibility and dicrotism. Intense sweating may occur, the patient being bathed in perspiration.

The tongue is dry and as a rule rather characteristically furred, there being a red tip, red edges and central red channel with two separate patches of thick white or yellowish-white fur. In bad cases the regular dry, brown, furred, cracked tongue of typhoid is in evidence. There is little in the way of abdominal symptoms save a certain elasticity of the abdominal wall, and the spleen is usually not palpable. There may be tenderness in the left hypochondrium, and percussion not infrequently indicates enlargement of the spleen. The liver is not enlarged nor, save in paratyphoid A infections, is the gall bladder painful in uncomplicated cases.

Rose spots are very commonly seen. They come out in crops at intervals of three to seven days, probably as a rule between the seventh and tenth day, and last for three or four days. In a good many cases they are only present after the temperature has fallen to normal. When fully developed the spots are distinctly larger, redder, and more lenticular than those of true typhoid. Sometimes they remain of the typhoid type. Their favourite sites are the lower ribs in front, the flanks and the back of the shoulders. When profuse they are scattered over the abdomen, and may be minutely vesicular or have an acne-like appearance. In number they may vary from half-a-dozen to well over a hundred. It is said that in paratyphoid A infections the rash tends to be very profuse and may somewhat simulate that of measles. In paratyphoid B the rash is distinctly papular but markedly pleomorphic, the papules varying in appearance.

Some bronchial catarrh is often present, but severe bronchitis is not common.

It is to be noted that moderately severe cases often markedly improve a few days after admission to hospital, and this quite apart from any treatment beyond dieting and nursing. The usual fall of the temperature by modified crisis or short lysis is shown in the charts. Relapses are not uncommon, and this is specially true of paratyphoid A, where they may be associated with rigors. A case is on record where a relapse occurred thirty-nine days after the temperature had reached normal. There are slight and more severe forms. The latter are more or less recrudescences of the disease.

Actual re-infections are rare. A chronic form of paratyphoid B has been described in which the disease lasts as a septicæmic condition for a long period, it may be several months.

Paratyphoid C.—Paratyphoid C differs from the other paratyphoid fevers in certain important respects. The causative organism is closely related to *B. suipestifer*, and at one time the two organisms were considered identical. Outbreaks of paratyphoid C develop most readily in a community already affected by some other disease, and in the past epidemics have been recorded in association with malaria and relapsing fever. The infection is essentially a septicæmia without involvement either of the intestine or of the mesenteric glands. The causative organism can be isolated from the blood without difficulty, and seemingly at any stage of the disease. Fever may last from a few days to six weeks or thereabouts, and the temperature curve is very variable in type—continuous, with marked remissions, or even intermittent. There is a peculiar liability to localized septic complications in the form of cold abscesses due to *B. paratyphosus* C. Any part already weakened by trauma or by some other infection may be involved. Such abscesses have been recorded in the liver, gall-bladder, in joints, etc., and at the site of intramuscular injections of quinine.

Morbid Anatomy.—The following points are of interest :—

1. The lesions may be the same as in typhoid fever.
2. The large intestine is more commonly ulcerated than in typhoid fever.
3. The intestines may be acutely inflamed throughout their length, but the lymphatic tissue may escape.
4. There may be no change at all in the intestines. This is the rule in paratyphoid C.

Prognosis.—This is good except in cases showing meteorism, severe bronchitis, certain other complications, or, and this is important, a persistently rapid pulse, *i.e.* above 100. At the same time it is well to remember that there are very severe and fatal forms of both types of infection.

Complications.—Jaundice may mask a paratyphoid infection, and should always be regarded with suspicion. A considerable number of complications are mentioned, the more important being hæmorrhage, perforation and femoral thrombosis. The tendency for paratyphoid B infections to involve the large bowel and to be associated with abscess formation must not be forgotten. A case complicated by cerebral abscess has been recorded. Tachycardia may be troublesome during convalescence. Most of the complications met with in typhoid fever may also occur, but less commonly, in the paratyphoids. Perforation and the classical typhoid state are but rarely seen.

Diagnosis.—The bacteriological diagnosis is of great importance. Except in paratyphoid C, blood culture as a rule is only positive at the beginning of the disease. The value of the agglutination reaction in paratyphoid has certainly not been enhanced by antityphoid inoculation, but this is a matter which cannot be here considered. A leucocyte count will show leucopenia. A long series

of negative examinations of the stools must be made before paratyphoid infection can be excluded, and even then the bacillus may be missed. It is rarely found in the urine.

Differential Diagnosis.—In the Mediterranean war area, apart from true typhoid, the disease most often mistaken for paratyphoid was dysentery. There is not much excuse for such a mistake, and if medical officers were more careful to view the stools of their cases this error would not so frequently occur. Other faulty diagnoses which have been noted are jaundice, influenza, especially gastric influenza, bronchitis, rheumatism, tuberculosis, undulant fever, cholecystitis and appendicitis. The condition is liable at its outset to be confused with phlebotomus and dengue fever and malaria by those unfamiliar with these diseases. *B. coli* septicæmia may simulate it, and can only be diagnosed definitely after bacteriological examination, while a so-called infective gastro-enteritis, possibly due to *B. coli communis* and in which the whole dorsum of the tongue is furred, may closely resemble paratyphoid.

Prophylaxis.—As for bacillary dysentery. In addition to T.A.B. vaccine special hygienic supervision of meat is required to lessen the risk of infection with *B. paratyphosus* B. This applies especially to all forms of pork, but it is probable that many outbreaks of food poisoning attributed to *B. paratyphosus* B in the past were really due to *B. ærtrycke*, which is indistinguishable except by detailed bacteriological analysis.

Treatment.—As for typhoid fever. Enemata are indicated in the earlier stages. Aspirin often relieves headache and hypnotics are sometimes required. Barbitone in two 5-grain doses in hot tea or as a tablet checks the profuse night sweat. Murphy's method of administering, drop by drop per rectum, a 6 per cent. cold solution of glucose has been highly recommended as an anti-thermic measure which has an excellent effect on the patient's general condition. Thirty to 40 drops are given a minute, and as much as 3 quarts may be administered in the twenty-four hours. A single injection occupies an hour to an hour and a quarter. Vaccine therapy may be employed. The action may not be specific, but owing to changes as the result of injecting a foreign protein ; at least, this appears to explain why paratyphoid cases benefit when given intravenously vaccines consisting chiefly of typhoid bacilli. Liquid paraffin can safely be given in most cases to counteract constipation, but no purgative should be allowed. A liquid diet based on milk is advisable during the febrile period in all but the very mildest cases. Plain or milk chocolate (nut chocolate must, of course, be avoided) is an excellent food and provides a little much needed biting exercise. Boiled fruit drops, especially acidulated drops, help to keep the mouth clean and promote the flow of saliva, thus diminishing the danger of suppurative parotitis. Fruit drops must on no account be given to semi-conscious or drowsy patients as they may be swallowed whole or inhaled.

It should be noted that many physicians now adopt, with apparent good result and no increase of disasters, a far more generous diet than was formerly considered safe. In spite of this, great care must be exercised in the choice of diet during and for a few days after the febrile period.

PELLAGRA

This is a chronic non-infectious disease, occurring amongst those taking a diet deficient in certain essential protein factors. It is especially likely to affect maize eaters. Clinically it is characterized by buccal changes and gastro-intestinal disturbances, nervous and psychical features and a symmetrical erythema affecting skin exposed to the sun's rays and to friction.

Geographical Distribution.—Since the year 1778 pellagra has been found to exist in nearly every country adjoining the Mediterranean and Black Sea littorals, and further afield, in Portugal, Central America and the southern part of the United States. Although its main incidence has hitherto been confined to the above regions, cases have also been reported from Japan, China, the Straits Settlements, some of the islands of the West Indies, Germany, Poland, India and Great Britain.

Hypotheses of Causation.—In a disease, the exact cause of which remains unproved, and concerning which there is a mass of speculative literature spread over two centuries, many hypotheses about its probable cause have naturally been put forward from time to time. Of these the most important are :—

(*a*) Infecting agent.
(*b*) Some deficiency of the diet, embracing :—

  (i) Deficiency in the standard of protein and its biological value, and
  (ii) Toxic (non-infective) agent acting in conjunction with deficiency of the diet.

People of any race, age or sex are susceptible; the malady is, however, more common amongst the poorer classes. The highest incidence of the disease is in the spring months. It affects specially maize eaters and those living on vegetable proteins of low biological value. The administration of nicotinic acid, and its amide, bring about a rapid improvement of the symptoms of pellagra. This discovery has very greatly facilitated the treatment of severely ill pellagrins.

Pathology.—There is a general wasting of all the tissues, including the thoracic and abdominal viscera. The most important changes occur in the gastro-intestinal tract: the whole tract shows atrophic changes of the mucosa. The liver and spleen are usually shrunken and atrophic. Areas of skin exposed to sunlight or friction are thickened and the surface rough. The changes in the nervous system, though slight, are widespread—brain, cord and peripheral nerves may all be involved to some extent in severe cases. There is, however, no abnormality in the cerebro-spinal fluid. Gastric analysis has shown that more than half of pellagrins have a true achlorhydria not responding to histamine. Porphyrin is usually present in increased quantities in the urine even in the earliest stages of the disease and diminishes rapidly after the beginning of suitable treatment. The blood picture frequently shows some secondary anæmic changes; the total white count is unaffected, but there is usually a relative increase in lymphocytes.

Clinical Picture.

1. *Early Manifestations.*—The commonest early symptoms are dyspepsia accompanied by flatulence and sensations of burning or discomfort in the epigastrium. Nausea and vomiting is frequent and diarrhœa may be troublesome. Painful stomatitis and œsophagitis often occur. In some, nervous symptoms are noted early in the disease. These consist in mental irritability accompanied by intermittent headache and vertigo. There may be changes in character with loss of interest in family or business affairs. The well-known skin lesions are usually a later manifestation, and are not present during the early stages, though they may provide the first evidence to confirm the diagnosis.

2. *The Developed Syndrome.*—Here the clinical signs and symptoms fall into three main groups: those associated with the alimentary tract, the skin, and the nervous system.

Alimentary Tract.—It is common for the digestive symptoms to precede the nervous and for the skin lesions to appear some weeks or months later. The alimentary tract is commonly involved in its entire length. The tongue at first is flabby and large, showing indentations of the teeth laterally. It is furred in the centre and rather glazed elsewhere—a diagnostic sign. As the disease progresses the tongue becomes generally atrophied, the surface raw and eventually fissured. A diffuse inflammation of the mucous surface of the mouth is often present, sometimes associated with aphthous ulcers. Sordes at the angle of the mouth are seen in severe cases, with maceration and transverse fissuring covered with yellow crusts. Excessive salivation may be troublesome.

The early gastric symptoms are of discomfort only; later this becomes a persistent burning pain often associated with exces ive salivation. Anorexia may be a marked feature and nausea and vomiting are occasionally troublesome. Diarrhœa is an outstanding intestinal symptom.

Skin Lesions.—Changes in the skin usually occur after the gastro-intestinal and nervous symptoms are well established. They begin as a simple erythema resembling sunburn, confined to the exposed parts of the body or to situations subject to irritation. The lesions are symmetrical in distribution. Tingling and irritation is often complained of in the affected areas. The skin lesions show definite seasonal spring exacerbations and early lesions disappear completely in the cold months only to return the next spring. With the progress of the disease these skin changes become more marked; the early erythema gives place to darker pigmentation, the epidermis becomes thickened, inelastic, dry and scaly, or even fissured. In very acute cases the skin lesions may become moist and blebs, containing blood-stained serum, may develop on the surface of these areas. The blebs break down, leaving sores, which may become infected and produce large areas of cutaneous ulceration. Improvement in the skin lesions usually occurs with the onset of the cooler weather. Commencing in the centre of the affected skin areas the superficial layers of the unhealthy epidermis desquamate exposing atrophic pink skin.

The symmetrical involvement of the skin (Plate 24) usually takes place in the following order :—

(i) The back of the hands, including the knuckles.
(ii) The feet and ankles in those who go barefooted.
(iii) The forearms and legs.
(iv) The face lesions show a butterfly distribution, the affected malar areas being connected by skin involvement across the nose, sometimes extending up to the forehead, and
(v) The neck, showing a necklace or cravat distribution.

In addition to these areas any point of constant friction, such as the elbows, trochanters, knees, sacrum and sometimes the genital organs may show similar changes.

Nervous System.—Apart from the early mental changes, other very variable symptoms and signs may be found. Paræsthesiæ and numbness are often complained of in the lower limbs ; there is, however, seldom any objective sensory alteration. The deep reflexes are variable, sometimes being increased, especially in the early stages, in other cases difficult to elicit. Mental changes are often marked, the patient becomes dull, and the memory impaired. Later hallucinations may be present and the patient may pass into a manic-depressive state with suicidal tendencies.

Diagnosis.—In the established classical case the glossitis and gastro-intestinal disorders and symmetrical skin lesions make the diagnosis easy. In the early stages, however, it may be difficult to establish the diagnosis definitely. A careful history as to dietary deficiency is important. Harris and Raymond's urinary test for nicotinic acid excretion may be of value in doubtful cases. The buccal changes resemble those in sprue, but fæcal analyses easily separate these two diseases.

Treatment. *Prophylactic.*—A well-balanced diet containing meat, eggs and milk will prevent the development of pellagra.

Curative.—If the disease is established, rest in bed is necessary at the commencement of treatment. The patient should, if able to digest a full diet, be given food rich in animal proteins and vitamin B_2 (riboflavine). Lean underdone meat, liver, eggs, and fresh milk and fresh fruit and green vegetables contain these essential ingredients. Such a diet will quickly bring about an improvement in the mild or moderately severe cases. Active preparations of B_2, such as brewers' yeast, wheat germ or Marmite, can, with advantage, be added to this diet. The discovery of the curative value of nicotinic acid has been of the very greatest assistance in the treatment of pellagra, especially in the severe cases unable to digest and assimilate sufficient of the necessary curative articles of diet. The glossitis, gastro-intestinal and mental symptoms very quickly respond to this form of treatment. Nicotinic acid is best given by mouth in daily amounts of about 500 mg. in divided doses during the day. The dose should be decreased as improvement takes place. No serious toxic effects have resulted; occasionally, however, the patient may experience flushing and a burning sensation of the skin, or gastro-intestinal symptoms, nausea and vomiting. These symptoms are avoided if nicotinamide is given instead of nicotinic acid. Where neuritic lesions are present benefit will result from administration of B_1 (thiamine) by daily injection of 50 to 100mg.

PHLEBOTOMUS FEVER

(Sandfly Fever)

This specific fever of short duration has a wide geographical distribution in Southern Europe, India, Africa, North and South America and elsewhere. The infective agent is an ultramicroscopic organism which is introduced by the bite of a minute hairy insect, popularly, though erroneously, known as a sandfly; hence the synonym sandfly fever. Pappataci fever and three days' fever are other terms for the disease.

The Vector.—The proven vector is *Phlebotomus papatasii*, but it is probable that other species are capable of conveying infection. It is a small hairy midge (Fig. 17). As *Phlebotomus* passes the winter in its larval stage, the fever is a disease of the summer months.

The breeding-places of the fly are the interior of rubble and stone walls, crevices of caves and dug-outs, cracks and fissures in artificial embankments such as the earthen parapets of trenches, walls of old cellars as in the case of Sedd-el-Bahr at Cape Helles, amongst heaps of damp stones, bricks and tiles, and also in the surface soil. In all cases slightly moist organic matter is essential for breeding, and associated with this material there must be some crack or fissure providing the necessary protection, darkness and moisture.

The adult flies shelter in similar situations, in clods of earth, beds of streams and holes in trees. It is worthy of note that they may be carried in timber and other cargo from place to place by sea-going vessels, a matter of some importance in districts where hospital huts, cooking sheds, wooden latrines, etc., are being erected.

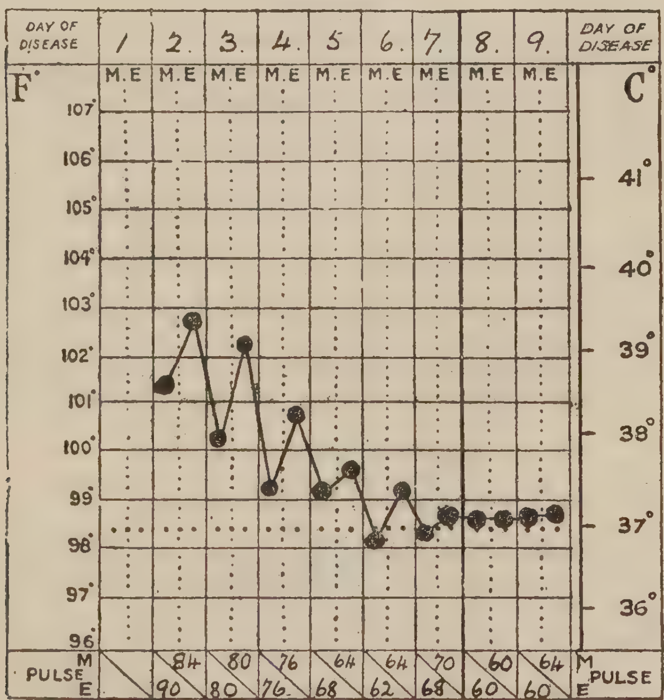
Towards evening the flies sally forth upon the blood quest, the females alone being bloodsuckers and feeding principally in the gloaming and at dawn. They chiefly attack the wrists and ankles and can easily bite through thin socks or light cotton and linen clothing. A single fly may make many punctures and becomes sluggish after several suctions. One fly can infect.

At sunrise they vanish, either retiring to their breeding haunts or seeking dark corners in rooms or dug-outs. They dislike sunlight, but are attracted by lamps and candles. It is probable that they rarely traverse more than fifty yards or so and they do not fly high. The bites are painful and, when numerous, the bitten part may be badly swollen. Vesicles may form resembling those of chicken-pox. An attack by many flies effectually prevents sleep.

The Fever.—It is short and sharp. Incubation period two to seven days. Attack usually sudden, commencing with a feeling of chilliness and malaise. There may be rigors, but these are never so severe as those of malaria. Vertigo, very severe frontal headache, pain at the back of the eyes, accentuated by pressure on the globes and the least movement of the head, pains in the back and legs like those of influenza, and general stiffness of the muscles soon prostrate the patient, who becomes drowsy, irritable if roused, but suffers from insomnia. The face is very flushed and may look swollen.

This flushing may persist long after the fever is gone. The conjunctivæ are injected so that the appearance resembles that sometimes seen in mastiffs or bloodhounds, hence the original name of "dog disease." There is no lachrymation or catarrh as is commonly present in influenza. Anorexia with pain or discomfort in the pit of the stomach is a feature and constipation is the rule, though diarrhœa sometimes occurs, as does vomiting. The tongue, clean at the tip and edges, is coated elsewhere by a thin white or brown fur. The fauces and palate are often congested and may exhibit small vesicles for which it is always well to look. Castellani describes small hyperæmic, roundish spots on the palatal mucosa. Epistaxis is not infrequent at a late stage of the illness. The skin is generally dry and even harsh, but may be moist. Apart from the face flush, which may involve the neck and upper part of the chest, there are no rashes, but these may be simulated by the numerous bites of the sandflies which, possibly as the result of scratching and irritation, may assume the appearance of a severe lesion, even simulating the exanthem of chicken-pox. Typical temperature records are shown. The rise is rapid. By the evening of the first day's fever a temperature of 101° to 103° is reached. It remains elevated for about twenty-four hours and then begins to fall, descending gradually on the third and fourth days and thus terminating very differently from the crisis of an ague fit (Figs. 55 to 57). An after-rise of temperature is by no means uncommon in some outbreaks, but is usually slight and much less marked than that of dengue. The pulse rate throughout is comparatively slow and the

Fig. 55.



Type of Temperature in Phlebotomus Fever.

Fig. 56.

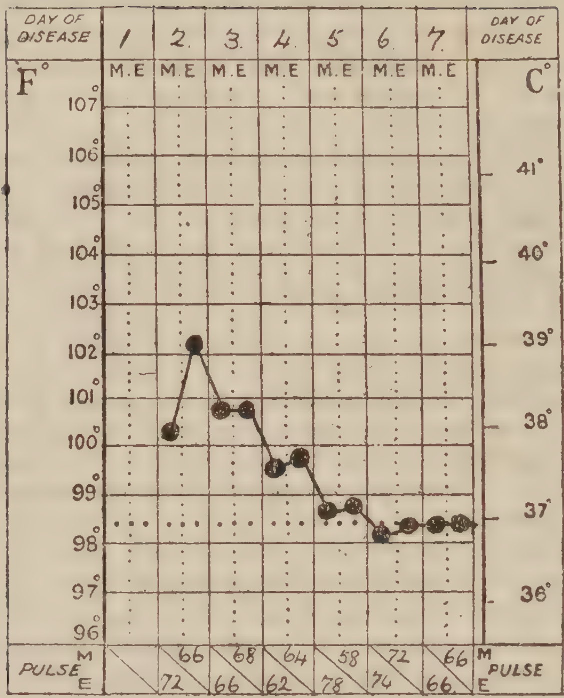
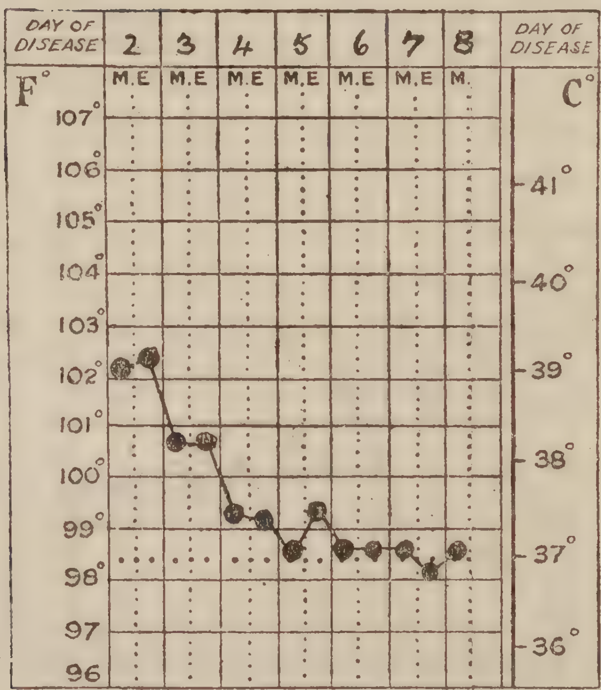


Fig 57



Varying Types of Temperature in Phlebotomus Fever.

blood picture is rather typical, *i.e.* a leucopenia with a relative decrease in the polymorphs. The eosinophiles diminish during the fever, but increase after it.

The patient may get better rapidly, or convalescence may be protracted and characterized by mental depression, lethargy, dyspepsia and insomnia; the sense of taste and smell may be lost for a time. Recovery appears to be the invariable rule. The blood is only infectious during the first forty-eight hours of the illness and the infected sandfly only becomes capable of transmitting infection after the lapse of six days.

Differential Diagnosis.—A disease which closely simulates this fever is paratyphoid, especially in its early stages and milder forms, but abortive enteric, dengue, malaria, undulant fever, typhus, heat-stroke, and influenza may be mistaken for it. In dengue rashes are present in 70 per cent. of the patients; in typhus there is usually a leucocytosis; in influenza respiratory catarrh is a marked feature.

Prevention and Treatment.—(*See also* "Arthropod Pests.") Under active service conditions it is rarely feasible to make use of fine-mesh muslin as a measure of protection, to trap the adult flies or to deal with breeding-places. Spraying of tents, rooms, dug-outs, etc., may be feasible and is likely to be of value. Tobacco smoke is useful. All that can usually be done is to employ repellants.

When it can be managed camps should be placed on high-lying sites exposed to the wind and should be well away and up-wind from horse lines.

Treatment is entirely symptomatic.

Quinine is useless and may aggravate the symptoms. Aspirin and the salicylates in fairly large doses often afford comfort. Severe myalgia is benefited by the application of hot sandbags.

Cases treated in endemic areas in hospital should be surrounded by fine-mesh nets to lessen the risk of others becoming infected.

This is a wise precaution, although Whittingham and Rook have demonstrated that phlebotomus fever may be propagated by *P. papatasii* bred in a non-endemic area, infection apparently having been acquired from the parent flies.

It should be remembered that newcomers to tropical or semi-tropical countries in which sandfly fever is endemic are more susceptible to the disease than others. Consequently, in selecting units for operations in a sandfly fever area during the sandfly season, those should if possible be chosen which have been "salted" by a residence of two or three years in the endemic area.

PLAGUE

Plague is endemic in parts of India, China, Africa and elsewhere. Epidemics are of common occurrence, and sporadic cases of the disease may crop up anywhere, especially amongst persons coming in contact with natives, and in the neighbourhood of docks.

Etiology.—The disease, which is primarily an epizootic in rats and other rodents, is due to the bipolar-staining, Gram-negative *Pasteurella pestis*, and in its bubonic form is conveyed from rat to

man mainly by the rat flea, *Xenopsylla cheopis* (Plate 25), though other fleas are known to be effective vectors.

The freedom from plague of parts of India has been attributed to the predominance of *X. astia* on the rats in such districts. Under similar conditions this species appears to be a less efficient vector of plague than *X. cheopis*, and Hirst has shown that it bites man reluctantly at temperatures over 80° F. As *X. astia* is a hot weather flea, some consider that its prevalence merely indicates meteorological conditions which are unfavourable to the spread of plague. Both the grey rat, *Rattus norvegicus*, and the black rat, *Rattus rattus*, fall victims. No reliance should, however, be placed on these colour distinctions as both *R. norvegicus* and *R. rattus* may be brown. The former is the usual ship rat, and in both species plague occurs as an acute and chronic infection. The black rat is the more dangerous, as it lives in closer association with man.

Animals other than rats may serve as reservoirs of infection, and in recent outbreaks of plague in Africa the various small mammals responsible were incriminated only after considerable research.

It is worth noting that the domestic animals, in times of epidemic, may suffer from pneumonic plague and become sources of infection. Virulent plague bacilli were isolated from the lungs of donkeys in North Manchuria, and camels have been known to infect man.

It is now recognized that certain forms of merchandise, especially grain and to a lesser extent raw cotton, because of the transported rats and fleas, are more to be dreaded as vehicles of plague infection than the human being *per se*.

There is some evidence to show that bed-bugs may be operative in spreading bubonic plague, but their rôle is certainly a minor one. Living plague bacilli have been found in human lice (*Pediculus humanus*), and it is thought possible that infection may be conveyed as a result of the habit of certain tribes of crunching lice between their teeth and swallowing them.

Pneumonic plague is transmitted from the sick to the healthy by droplets of sputum expelled in coughing, and also apparently by the invisible spray which pneumonia patients discharge from the mouth. There is some evidence to show that, in the case of primary septicæmic plague, infection may take place through the gastro-intestinal tract.

There are thus three recognized forms of plague and of infection.

The bacilli swallowed by the flea in feeding on infective blood multiply at its proventriculus, and the bacillary mass eventually extends into the œsophagus, thus blocking the entrance of the stomach. The starved flea makes violent efforts to get more blood, and the œsophageal contents regurgitate, thereby infecting through the skin lesion the healthy person on whom the flea is trying to feed. The flea itself does not necessarily die from the obstruction, but it is apt to do so if the weather is dry, presumably from lack of fluid. In this connexion it is interesting to note that plague does not maintain itself in epidemic form when the temperature rises above 80° F. accompanied by a saturation deficiency of over 0·30 of an inch (Brooks).

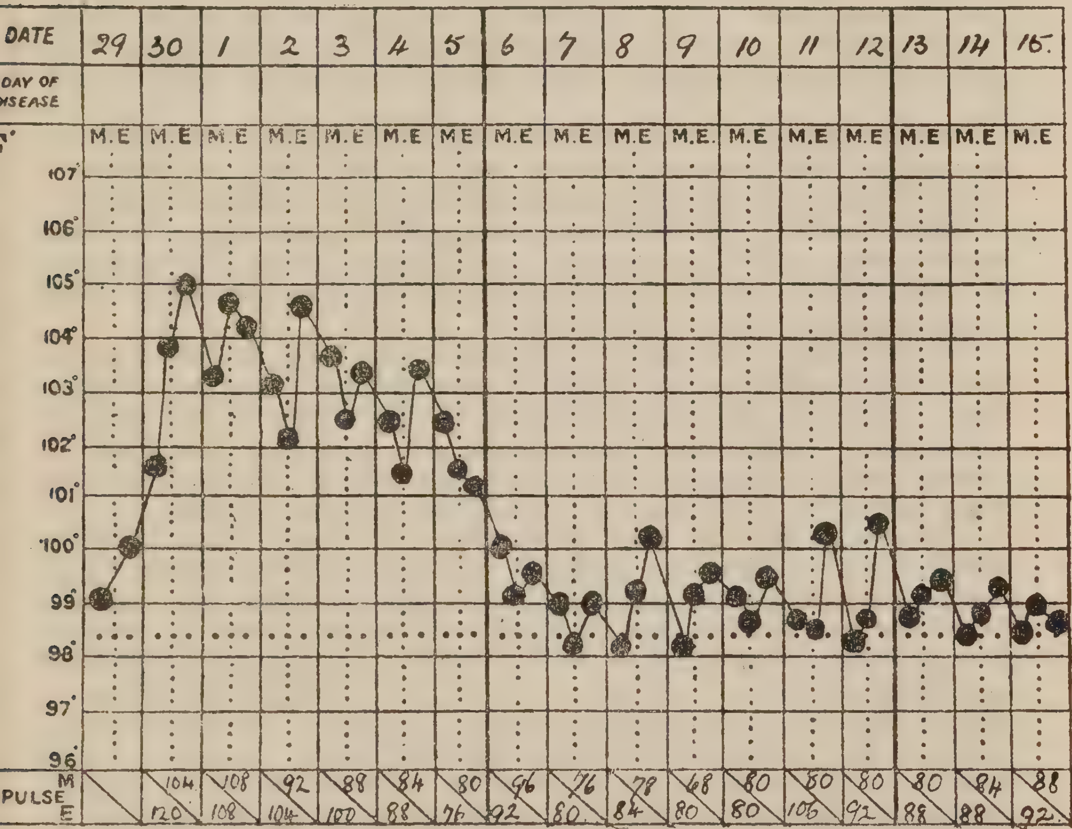
Infection may also occur from the bacillus-containing fæces of the flea voided on the skin and rubbed into the wound.

When rats become ill or die, the fleas leave them and attack man. This is specially true when the epizootic is amongst black rats. Certain rat fleas may remain infective for at least six weeks.

Symptoms.—The incubation period is from two to eight days. Rarely it may be extended to fifteen days, but a quarantine of ten days is usually considered sufficient. Prodromata are rare.

There is an ambulatory form, or pestis minor, in which the fever and prostration are slight. There may be some swelling and tenderness of the lymphatic glands, and there is usually at the site of the

Fig. 58.



Bubonic plague. (After Simpson.)

flea-bite the primary vesicle or pustule. It is very important to search for this and have it examined bacteriologically. Patients with pestis minor may suddenly collapse. They are dangerous, for they act as carrier cases.

All three forms of pestis major present certain symptoms in common, *i.e.* sudden onset, sharp fever, vertigo, great prostration, a drunken gait, appearance and speech, and great cardiac weakness.

Bubonic Plague.—The patient suffers from headache and drowsiness and his face is pale and anxious. His features become drawn

and haggard, his eyes bloodshot, sunken and staring, his expression often one of fear or horror. If still able to walk, he drags himself along like one in a maze or staggers about like a drunken person. As the fever increases his face gets hot, flushed, and bloated and his pupils dilate. The fever curve, as seen by the chart (Fig. 58), is irregular and the pulse is rapid and weak. Thirst is intense, the furred tongue becoming dry and brown and sordes accumulating about the teeth, lips, and nostrils. Delirium, and even convulsions, may ensue. The spleen and liver are enlarged, the urine scanty but rarely definitely albuminous.

About the second or third day the characteristic bubo or buboes develop. The bubo is most commonly inguinal, as the word indicates, but the axillary, submaxillary, cervical, or other glands may be involved. As a rule there is only one bubo, which varies from about the size of a walnut to that of a goose's egg. The œdema of the surrounding tissue makes it look larger than it really is.

This marked local reaction is a favourable sign. Small, hard buboes indicate a severe infection, and the shrinking or disappearance of buboes which have commenced to form is a lethal prognostic. "White buboes," *i.e.* those unaccompanied by any sign of inflammation other than the swelling, are of grave omen. Pain varies but may be very severe ; sometimes it is complained of before there is any external evidence of the bubo.

In cases which are going to recover, improvement sets in about the fourth or fifth day and is often signalized by a profuse perspiration. As a rule the bubo continues to enlarge and soften, and, if not incised, bursts and discharges pus and sloughs. Sometimes it resolves without suppuration. From the sixth to the tenth day the temperature becomes normal and the patient convalescent.

Epidemics vary in their symptoms. In some, hæmorrhages, which may be petechiæ or large purpuric spots ("tokens") or definite bleedings from the nose, stomach, intestines, etc., occur ; in others, gangrenous areas of skin form over and about the buboes or elsewhere ("carbuncles") ; in others, pulmonary congestion and inflammation are present. In a small percentage of cases, plague blains may be a marked feature. These are superficial blebs, white or dark in colour, and swarming with bacilli. Carbuncles and blains usually indicate a heavy infection. Tokens invariably presage death—Shakespeare's "tokened pestilence where death is sure."

When a case ends fatally death usually takes place between the third and fifth days.

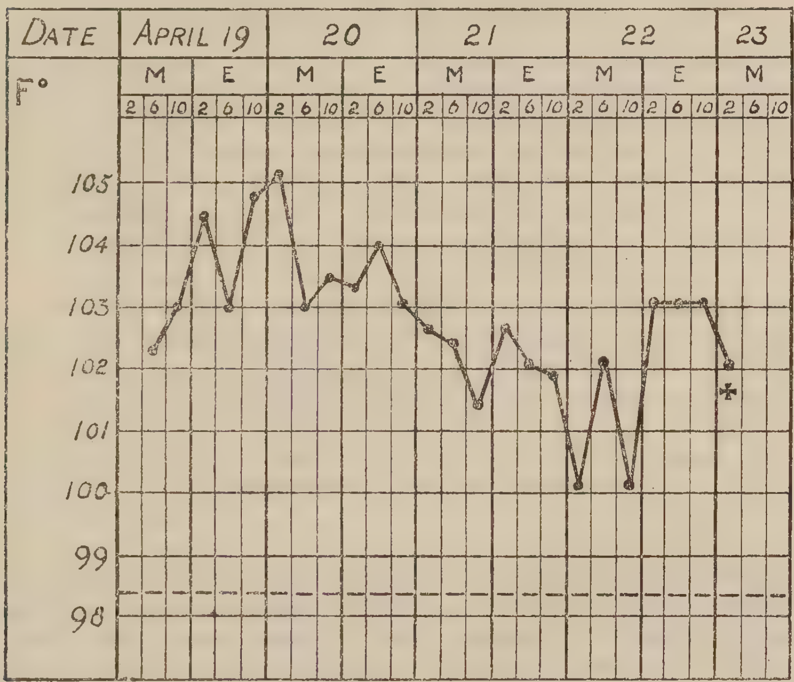
Pneumonic Plague.—Rigors and vomiting often characterize the onset. Cough, dyspnœa, and cyanosis occur, accompanied by a profuse, watery, blood-tinged sputum, which is quite unlike the rusty, tenacious sputum of ordinary lobar pneumonia. This plague sputum teems with bacilli and is exceedingly dangerous. The patient never has a chance. Moist râles are heard over the bases of the lungs, the toxæmia is intense, the breathing rapid, and death speedily ensues. The type of temperature is shown in the chart (Fig. 59).

Septicæmic Plague (Fig. 60).—In the primary form the patient

is at once rendered prostrate. His pulse speedily becomes thready or imperceptible at the wrist, he is pale and apathetic, and his temperature, owing to the magnitude of the infection, may scarcely rise at all. Hæmorrhages often occur and stupor, coma, or delirium herald speedy death. There have been cases where intense headache and fever were the only signs and where the patients died within forty-eight hours.

Complications.—Pneumonia, toxic degeneration of the heart muscle, prolonged suppuration of buboes, iritis, corneal ulcers, and, in rare instances, blindness.

Fig. 59.



Pneumonic plague. (After Simpson.)

Morbid Anatomy.—All that need here be mentioned is the marked involvement of the lymphatic system and the destructive action of the plague toxin on the endothelial lining of blood-vessels and lymphatics.

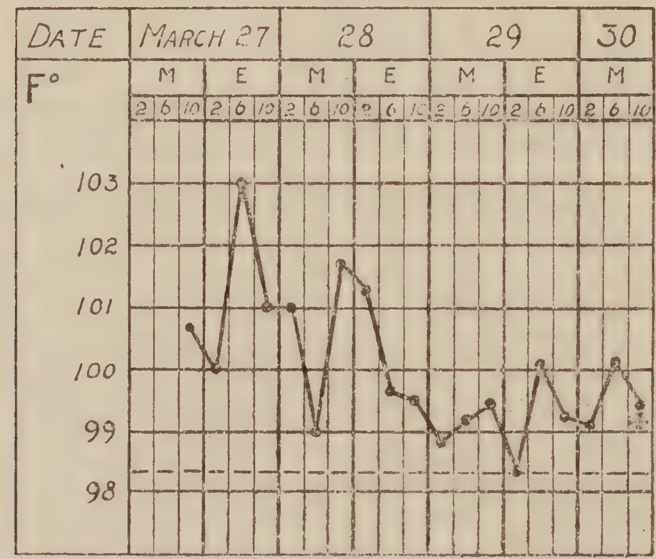
Differential Diagnosis.—The disease most like plague in its early stages is typhus fever. In both there is the same mental hebetude and drunken aspect, but the course of the illness and the bacteriological examination soon clear up the difficulty. A venereal bubo may be mistaken for a plague bubo, a fulminant case of enteric for early bubonic plague, and an influenzal pneumonia for pneumonic plague.

An ordinary septicæmia, some varieties of relapsing fever and a pernicious type of malaria may simulate septicæmic plague. It is

worthy of note that mixed cases of plague and relapsing fever are not uncommon.

Prophylaxis—Personal.—Inoculation with Haffkine's or Kolle's vaccines affords some protection for a few months and is recommended in face of an outbreak. Haffkine's vaccine is usually given in a single subcutaneous injection of 4·0 c.cm., and this is liable to cause an immediate febrile reaction, and occasionally a delayed

Fig. 60.



Septicæmic plague. (After Simpson.)

reaction with lymphadenitis ten days later. Kolle's vaccine is given in two doses, of 2,000 million and 4,000 million, at ten-day intervals.

Living "avirulent" plague vaccines have been used on a large scale in Madagascar and the Netherlands East Indies. They are effective but are not yet free from risk.

So far as bubonic plague is concerned, prophylaxis largely consists in warding off the attacks of fleas and bed-bugs. Pesterine is a good pulicide (*see* p. 21). Fleas dislike the smell of iodoform, but so do most people, and the free use of iodoform powder would probably lead to undesired isolation. Naphthalene alone or naphthalene in kerosene may be tried. Tricresol powder (3 per cent. cresol powder) has been strongly recommended.

Attendants on plague patients should wear leather or rubber gloves, overalls, and be protected about the feet and ankles by means of puttees or gum-boots. No food or drink should be partaken of in plague wards, and hand disinfection is essential. For a case of the pneumonic type, in addition to the foregoing measures, both patients and attendants should wear masks impregnated with disinfectant. All attendants should be given 20 c.cm. of anti-plague serum immediately, and at the same time injected with plague vaccine.

Mere drying of plague sputum is no evidence that the contained bacilli have been killed. Disinfectants employed in the dilutions usually recommended may fail to accomplish their purpose. A 1 in 10 solution of carbolic requires five minutes' contact to prevent the growth of *B. pestis* in sputum. The best disinfectant for the sterilization of the hands and gloves in plague work is methylated spirit.

For other measures as regards both fleas and bed-bugs, *see* section on Arthropod Pests.

Prophylaxis—General.—The usual quarantine period is ten days. The bacilli can persist in the bodies of recovered patients for three weeks; hence, to be on the safe side, convalescents should be isolated for a month.

The question of the destruction or disinfection of possibly infected fomites, such as clothes, skins, rags, etc., is important, for under certain conditions the plague bacillus possesses considerable vitality outside the body. Exposure of possibly infected bedding and clothes to the tropical sun is a valuable safeguard. An hour's exposure at 120° F. suffices to kill all fleas. It is of great importance to limit the food available for rats and to protect food supplies from their depredations.

Cats and dogs should be kept away from plague patients.

The great question of rat destruction cannot be here considered in detail, but, so far as the use of traps is concerned, mention may be made of the value of tomatoes as a bait for rats. Portions of tomato can also be treated with phosphorus paste or other poison. Scraps of fish are very attractive to rats.

R. rattus in India is most attracted by whatever grain forms the staple food of the district, and this should be used for bait. In hot weather fresh green vegetables, particularly cucumber, are useful. Traps should be oiled just sufficiently to prevent rusting and should not be washed overmuch, for cleanliness renders rats suspicious (White).

The use of baited birdlime spread on boards has in some places superseded that of traps, while extract of squills, of which one-tenth of a milligramme will kill a rat, and barium carbonate, have also been employed in rat warfare. White recommends the last should be used as follows: One pound of powdered native barium carbonate is mixed thoroughly with 3 lb. of flour made from the grain which constitutes the staple food of the locality. Sufficient water is added to make a fairly firm paste. This rolled into pill form is sufficient for 2,400 baits. These should be made fresh each day, and unconsumed baits collected.

For destroying rats and fleas on shipboard a Clayton apparatus is commonly used. It generates sulphurous acid gas under pressure; 3 lb. of sulphur for every 1,000 cubic feet is the usual allowance. A simple and rapid calculation is to allow 3 lb. for every 10 tons of gross tonnage. The fumigation is continued for twelve hours. Hydrocyanic acid gas is also employed and is very effective, killing both rats and fleas in very low concentration, but care must be exercised owing to its poisonous properties. The gas may be generated by the admixture of reagents in the following propor-

tions :—1 oz. NaCN, 1½ oz. commercial H_2SO_4, 2 oz. of water,* but for use on a large scale, special apparatus is required.

For the fumigation of rat burrows, etc., on land two calcium products are largely used. Of these, Calcid, is supplied in briquettes, each of 20 g. Each briquette contains calcium cyanide 88·5 per cent., pure lime 11·5 per cent. Cyanogen "A" dust contains 45 per cent. calcium cyanide, 55 per cent. slaked lime.

Both the above when powdered and exposed to air form hydrocyanic acid gas.

Rat guards must be fixed on mooring hawsers and cables, but have only a limited value. A good rat-catcher on board ship is much more useful.

As regards pneumonic plague the freest ventilation is necessary, for it is in close atmosphere saturated with moisture that infection most readily takes place.

Treatment.—The only treatment which is really of any avail, and then only in bubonic plague and when given early, is the administration of one of the anti-plague sera, of which Yersin's and Lustig's are the best known. The dose must be large, 50 to 100 c.cm. or more. In desperate cases it can be given intravenously. A more potent anti-plague serum has recently been introduced and good results are reported from its use. Drugs of the sulphonamide series have appeared to be efficacious in certain limited outbreaks of plague, but confirmatory evidence is desirable. The symptomatic treatment must not be neglected and is that for any severe febrile condition with certain special indications, such as the application of cold and of ichthyol ointment or belladonna and glycerine to the buboes, their careful incision once suppuration is established and their careful aseptic treatment.

Morphia is the best hypnotic. Cardiac stimulants are nearly always required.

Injection of iodine in the neighbourhood of buboes has been stated to do good. Some recommend intravenous injections of undiluted tincture of iodine, commencing with 7–10 minims twice a day; and mercurochrome, commencing with 30 c.cm. of a 1 per cent. solution, has been given by the same route.

Such methods of treatment require fuller investigation. Prognosis in plague is notoriously difficult, and the recovery of seemingly hopeless cases is likely to be attributed to whatever treatment happened to be employed. Moreover, as in other affections, a run of favourable cases may be encountered and mislead the observer as to the curative value of some medicament. For these reasons it is not uncommon to see some particular treatment vaunted as

* For the destruction of rats, 5 oz. NaCN are required (2 hours' exposure) ; Mosquitoes, 0·5 oz. (½ hour) ; Fleas, 2·5 oz. (½ hour) ; Lice, 10 oz. (2 hours) ; Bed-bugs, 5 oz. (1 hour) ; in each case for every 1,000 cubic feet. 0·5 oz. NaCN for every 1,000 cubic feet gives a theoretical concentration of 1 in 4,372 ; it is said a man can breathe 1 in 2,000 for 1½ minutes without ill effect. For fumigation on a small scale, the water is placed in the containers and the acid slowly added ; when everything is ready, the NaCN is dropped in either by hand, or preferably by some tipping device. Precautions are required to prevent splashing of the floor or adjoining walls. It is necessary to emphasize the absurdity of relying on any form of fumigation where unremediable structural peculiarities render a sufficient gaseous concentration impossible.

effective, usually on the evidence of a small number of cases. Up to the present, extended trials have failed to substantiate any of these claims. But this is an old experience in the history of plague. During the dreadful London epidemic of 1665 we find Boghurst writing with grim humour: "Mr. Garencières saith the Plague is the easiest disease in the world to cure, and soe said Mr. Stoakes the Apothecary . . . but hee is dead since."

RABIES

(Hydrophobia)

Rabies is a specific infective disease of the nervous system characterized by a long incubation period. The causative agent, which belongs to the group of filterable viruses, possesses all the characteristics that pertain to the filterable viruses in general.

Etiology—The disease occurs naturally as an enzootic among members of the canine tribe. The virus is present in the saliva of an infected animal, and man acquires infection in practically every case by being savagely attacked and bitten, although on occasions the infection may be transmitted by the animal licking an abraded surface.

In its distribution rabies occurs throughout most of the great continents of the world, from which, owing to the wandering habits of these animals, it is quite impossible to eradicate. On the other hand, on islands the disease can be eliminated. In the British Isles, for example, by rigid application of quarantine regulations and muzzling orders for dogs, the infection has successfully been stamped out. The disease occurs in any climate, and there does not appear to be any seasonal variation in its incidence.

Besides the canine tribe, certain other animals are natural vectors. In South Africa, meercats and genets are responsible for transmitting the disease, and in parts of South America and in certain islands of the West Indies, certain species of blood-lapping bats of the order *Desmodus* transmit an unusual type of rabies, the clinical picture of which is that of an ascending myelitis.

All warm-blooded animals are susceptible to infection, but it is from the dog and jackal that man is most frequently infected. It is of considerable importance, therefore, that all should be capable of recognizing the symptoms of this disease in the dog. The symptoms in the dog and in man are in many respects similar; indeed, all animals are in great measure affected alike.

The dog acquires infection from a rabid animal. When the virus is introduced into its body, and comes in contact with nerve tissue, it passes along the nerve trunks to the central nervous system where it develops. Having developed, it passes back along the nerves and can be demonstrated in the secretion of certain glands in the body, notably the salivary glands. The saliva is infective for a period of approximately ten days before symptoms of the disease are manifest. It is important to bear this fact in mind when dealing

with the question of persons who have been in contact with an infected dog.

The length of time the virus takes to travel from the site of the bite to the central nervous system depends upon several factors, the more important of which are the distance the bite is from the central nervous system and the size of the nerve trunk involved. The incubation period, consequently, will vary considerably. The period will, for example, be much shorter for implantations about the face than it will be for implantations about the leg.

Once the symptoms have become apparent, however, the disease runs a short course, usually of not more than five days and invariably terminates fatally. This is also of importance to bear in mind, since, if a dog is suspected of being rabid and is isolated for a period of ten days, and at the end of this period is alive, it is safe to assume it has not been suffering from rabies. This test may be applied when there are no facilities for laboratory diagnosis.

Pathological Changes in the Infected Dog. *Naked-eye Appearances.*—There are no naked-eye appearances pathognomonic of this disease, although a striking feature is the marked degree of emaciation presented by a dog that has died from this infection. It is much greater in degree than can be accounted for by the inability of the animal to partake of food during the short course of the disease. The distinctive change is confined to the brain and for this reason a general post-mortem examination is not necessary.

Microscopical Changes.—The demonstration of "Negri Bodies" is conclusive evidence of rabies, for in no other disease are these characteristic features found. Negri bodies are cytoplasmic inclusions, and are found in their most highly developed form and in greatest number inside the large pyramidal cells and their processes of the hippocampus major.* For this reason the hippocampus major is regularly examined for the presence of these specific bodies. It is of considerable importance, therefore, that every medical officer should know where this structure lies and how to expose it.† Negri bodies may be found in any of the neurons of the nervous system, but rabies cannot be excluded in the laboratory unless the hippocampus major has been examined.

Symptoms in the Dog.—The symptoms in the dog, with certain exceptions, are similar to those that occur in man. The course of the disease, from the time when the symptoms commence, lasts not more than five days, and during this period there are three stages.

(1) *Premonitory Stage.*—The characteristics of this stage are: altered behaviour, the dog seeks secluded corners, ceases to be obedient or may show excess of affection; perverted appetite,

* The hippocampus major in the dog is a relatively large structure and forms a prominent elevation on the floor of the descending horn of the lateral ventricle and is strongly curved in conformity with the course taken by the horn in which it lies.

† To expose the hippocampus major the brain is laid down vertex uppermost and the upper parts of one hemisphere are removed in thin horizontal slices till the anterior part of the lateral ventricle is reached. The roof of the ventricle is then cut away an the hippocampus will be recognized as the laterally arched ridge which forms the floor of the ventricle.

this is one of the most characteristic features of the disease in all the lower animals. These early symptoms may not always be pronounced, and this makes it difficult to recognize the disease at this stage, especially if there is no suspicion of any infection.

(2) *Stage of Excitement.*—This stage is characterized by aggression, snapping, unprovoked biting, aimless wandering and alteration of the bark to one of a high-pitched tone. Later, there is a staggering and erratic mode of progression, panting and outpouring of unswallowed saliva from the mouth. This is the " mad dog " stage and lasts for one or two days.

(3) *Stage of Paralysis.*—If the stage of excitement is short, dumb rabies may supervene without the furious stage ever having been observed. The paresis commences in the hind extremities, particularly noticeable in the tail which hangs down in a lifeless manner. Later, the animal squats down on its hind quarters, emitting the characteristic bark with thick ropy saliva streaming from the mouth. Ultimately the paralysis involves the anterior extremities and the animal falls and lies in a helpless state. The smallest stimulus, such as a puff of cold air, may cause the animal to exhibit muscular spasms which affect the whole body.

The Disease in Man. *Incubation Period.*—The period of incubation is variable and is dependent upon a number of factors, but it can be stated generally that the nearer the bite is to the brain the shorter will be the incubation period. The figures usually given are as follows: For bites about the face, thirty days; the arm, forty days; the leg, sixty days. It must, however, be emphasized that these figures are subject to wide variation—from seventeen days to three months or longer.

Onset.—There may, in some cases, be a prodromal stage with slight rise of temperature, and during this period the patient may complain of slight headache and insomnia, but more frequently the onset in man is sudden.

Symptoms.—During the short course of the disease three stages may be distinguished. More often, however, these stages are ill-defined, the end paralytic phase developing rapidly.

(1) *Premonitory Stage.*—The site of the bite often becomes irritable with pains in its neighbourhood. Fear and anxiety are often prominent in those who are aware of the possibility of their condition. There is depression with a desire for solitude, and intolerance to loud sounds and similar stimuli with periods of irritability. The voice becomes husky and difficulty in swallowing develops. This stage may last one or two days and gradually merges into the next phase.

(2) *Stage of Excitement.*—This stage is characterized by marked irritability. The tendon reflexes are exaggerated, and if the patient be observed, an expression of terror can be seen on his face. The condition progresses to one of hyper-excitability. The mind is clear, however, and if the attention of the patient is fixed he can, for a short period, control himself.

This sudden change is, on occasions, most dramatic, and must be seen to be appreciated. As the disease develops these periods of calm become progressively shorter and the patient merges into a state of extreme excitability with spasms evoked by any stimulus. These spasms affect the pharynx and larynx and respiratory muscles first, and ultimately the whole body. Pharyngeal spasms are specially liable to be brought about by any attempt to drink (hydrophobia). Even the sight or mention of water may be sufficient to bring about a most distressing paroxysm. As the muscles of respiration become affected, breathing becomes laboured, noisy and a condition of air hunger develops. Later paralysis affects the throat with consequent difficulty in swallowing. The saliva becomes copious and viscid. Maniacal attacks may occur, but man rarely attempts to bite. The duration of this phase is one to two days and it merges imperceptibly into the next stage.

(3) *Stage of Paralysis.*—The paralysis becomes general and spasms cease. Consciousness usually remains till the end, but the duration of this phase is not many hours.

Course of the Disease.—From the time when the symptoms become apparent the course of the disease does not last longer than three to five days. No established case of rabies contracted from a dog has ever been known to recover. The regular order of events in man is that paralysis supervenes upon a state of excitement and death occurs either quietly or in the midst of a paroxysm.

Diagnosis and Differential Diagnosis.—Clinically there is little difficulty in diagnosing this disease. In the differential diagnosis the possibility of hysteria, tetanus, atropine poisoning and Landry's paralysis must be borne in mind. The laboratory diagnosis rests on demonstrating Negri bodies in the brain.

Treatment.—Treatment of rabies by vaccine therapy is not curative in the strict sense of the term, but preventive. Advantage is taken of the long incubation period in which immunity can be effected to abort the infection before it has had time to develop. But as immunity takes time to become established vaccine treatment should be commenced as soon as possible after the bite, and carried out whenever an individual has been bitten or contaminated with saliva, even though no wound has been inflicted.

Treatment comes under four headings: (i) Local; (ii) Vaccine prophylaxis; (iii) Serum prophylaxis; (iv) General.

(i) *Local.*—The wound should be washed thoroughly with soap and water and then cauterized. It is most important to reach every part of the wound and this is by no means an easy matter with deep bites. The cauterizing agents that may be employed are pure carbolic, concentrated nitric acid, silver nitrate, potassium permanganate or the actual cautery. For deep bites a knitting needle or similar piece of metal heated to a dull red heat makes a good cautery. It must be emphasized that local treatment does not do away with the need for specific vaccine therapy. Experimentally, it has been shown that the virus does not remain localized for any length of time.

(ii) *Vaccine Prophylaxis.*—This consists of a course of injections of anti-rabic vaccine.

The virus as it is recovered from an animal that has contracted the disease in the natural way has a great range of infectivity. It is termed the "street virus," and it is possible to modify its properties, in certain respects, by subdural inoculation of animals. When a suspension of this virus is injected into the rabbit subdurally, that is to say, injection by the shortest possible route, the symptoms of the disease appear in from fifteen to twenty days. As the virus is passaged by subdural inoculations from rabbit to rabbit, the incubation period becomes progressively shortened until there comes a time when the symptoms appear constantly on a particular day. The actual day of appearance depends upon the individual strain of virus, but for many of the strains the symptoms constantly become evident on the seventh day. When this occurs the virus is known as the "Fixed Virus." It differs from the street virus in certain respects, the more important of which is that it is less liable to establish infection in man on subcutaneous injection. On this account the fixed virus is the one that is used in the preparation of the anti-rabies vaccine.

Several methods are employed in the preparation of the vaccine, but they are all modifications, more or less, of the original method devised by Pasteur. This worker found that the spinal cords of rabbits dying of experimental rabies gradually lost their virulence when dried in the air over KOH. By inoculating dogs subcutaneously with cords dried for varying periods, beginning with the least virulent and working up to the most virulent, he was able to prevent the development of both experimental and natural rabies. The cords he injected first were avirulent; those for the later injections, virulent. In the treatment of human cases, he commenced with a cord that had been dried for fourteen days and gradually worked up to one that was only one day old. This treatment formed the starting point of a system of preventive treatment that has become of world-wide distribution. Pasteur's original method of inoculation is still used, but a number of other methods have been developed.

The vaccine used in India is prepared by the method suggested by Semple. It is a killed virus vaccine and consists of a carbolized suspension of brain tissue containing the fixed virus of rabies.

The dose of the vaccine administered varies according to the degree of risk attached to the bite. For this reason bites are classified according to their situation, severity and number.

The vaccine is administered by subcutaneous injection in the abdominal region. If the quantity to be given exceeds 5 c.cm. the injection is made in two places.

(iii) *Anti-Rabic Serum Prophylaxis.*—The use of anti-rabic serum as an adjunct to the routine vaccine treatment is at present under trial. The results, so far, are encouraging. The dose given is 20 c.cm. of the serum administered subcutaneously on each of the first two days of treatment, that is, a total of 40 c.cm. in addition to the appropriate doses of vaccine.

(iv) *General Treatment.*—No drug has been found to have any

effect on the course of the disease. To alleviate the symptoms the most useful drug is, perhaps, atropine because it reduces spasm, but any of the depressants may be used.

Complications following treatment with the Vaccine.—The local reaction which accompanies the milder degrees of treatment cause little inconvenience. But with the larger doses, there may be marked local reaction and considerable tenderness. Headache is a common complication and with patients suffering from chronic malaria the treatment may bring about a relapse of malaria. These complications are trifling, however, compared with the possibility of a neuroparalytic accident developing.

Neuro-paralytic sequelæ are not altogether rare and sometimes are fatal. They take the form of an encephalo-myelitis and range in intensity from a local paresis accompanied by paræsthesia to a rapidly ascending paraplegia of the Landry type. All intermediate stages may be seen. The onset of the symptoms calculated from the first day of treatment is nearly always within thirty days, and the earliest appearance of the symptoms may be within seven days of the commencement of treatment. The ætiology of this condition is imperfectly understood.

Laboratory Diagnosis of Rabies in the Dog.—The laboratory diagnosis is dependent upon demonstrating Negri bodies in the brain. The demonstration of the presence of the virus by animal inoculation is rarely carried out.

In handling a rabid dog it is important to remember that it is infective. Before removing the brain, therefore, the dog's head should be dipped in a bucket of strong disinfectant and the operator protected by wearing an apron, a pair of gloves and also goggles, if available.

Method of Removing the Brain.

1. With a hammer crack the skull bones through the intact skin.
2. Reflect the skin, remove the broken skull bones and expose the brain.
3. Incise the dura and divide the brain down the centre into two longitudinal halves.
4. Lift out each half of the brain separately after severing the nerves, and dispatch to the nearest military laboratory.

If the specimen is sent by post or rail, it must be preserved. The whole brain may be sent or the hippocampus major which forms the floor of the lateral ventricle.

Preservation of the Brain.—The fluids that may be used are methylated spirit or 10 per cent. formalin. The specimen should be wrapped in a layer of cotton wool, placed in a container of adequate size with a wide mouth and the lid sealed securely. The container should then be dispatched in a box with sawdust.

Prevention of Rabies in Animals.—Anti-rabic vaccine for animals is now available and gives protection for at least six months. It is advisable to have dogs inoculated whenever cases of rabies are known to have occurred in the neighbourhood. A similar course of treatment is given in the case of the dog as in man. If it is known, however, that a dog has been bitten by a rabid animal, it is better to run no risk and to have it destroyed.

RAT-BITE FEVER

A fever following the bite, especially, of rats, characterized by frequent relapses and caused by an infection with *Spirillum minus*, occurring naturally in rats, cats and other animals.

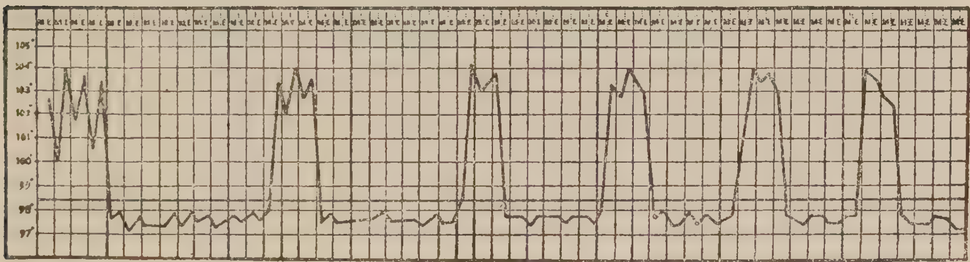
It occurs in every part of the world, but was first recognized in Japan where the disease is prevalent.

Spirillum minus measures usually 2 to 5 μ but sometimes up to 10 μ.

The coils are regular, varying in number with the length of the body from one and a half to two turns up to seven or eight in the unusually long varieties. Movement is facilitated by a group of flagella at each end.

Clinical Picture.—The bite usually heals normally in the first instance, but after a variable period from a week to months the scar becomes swollen, the lymphatics inflamed and the associated glands

Fig. 61.



Temperature chart in rat-bite fever.

enlarged and tender. At the same time constitutional symptoms manifest themselves by sudden pyrexia, headache, and chilliness and frequently pain in the joints and muscles are complained of. The temperature rises to 102° or 104° F., and with this a purplish maculo-papular eruption of widespread distribution usually appears and disappears with the fall of temperature. The fever lasts two to three days falling by crisis to rise again after a period of three to six days (Fig. 61). The constitutional symptoms improve during the apyrexial periods. If untreated many recurrences of pyrexia may take place.

Diagnosis.—This is usually easily made from the clinical picture and history of a bite. The rash may not be a prominent feature in some patients, especially if dark skinned. The spirillum may be demonstrated in the fluid obtained from the region of the bite either by dark-ground or stained specimen examination. They are usually very scanty in the peripheral blood. Inoculation of a susceptible animal is perhaps the most reliable method of demonstrating the cause of the illness. White mice, guinea-pigs or rats may be used for this purpose. A pre-existing infection of these animals must be excluded before using them for the test. 2 c.cm. of blood are re-

moved from the patient's vein and 1 c.cm. injected intraperitoneally into a young guinea-pig and 0·5 c.cm. into a white mouse. After a period of six days the blood and peritoneal fluid are examined daily under dark-ground illumination.

Treatment.—Response to arsphenamine compounds is very satisfactory, two injections usually bringing about a cure.

RELAPSING FEVER

(Including Central African Tick Fever)

This disease assumes its most virulent form and spreads with its greatest rapidity amongst a starved and debilitated population, whence the old name "Famine Fever."

Etiology.—It is probable that the organisms of relapsing fever were derived in the first place from small rodents, and conveyed to man by ticks. As a result of such casual infections, the organisms became adapted to a new transmitting host, the louse, and by the agency of this vector spread throughout the world. In this connexion it is suggestive that the spirochæte found in human relapsing fever in Dakar has been shown by cross-immunity experiments to be identical with a spirochæte of local shrew-mice.

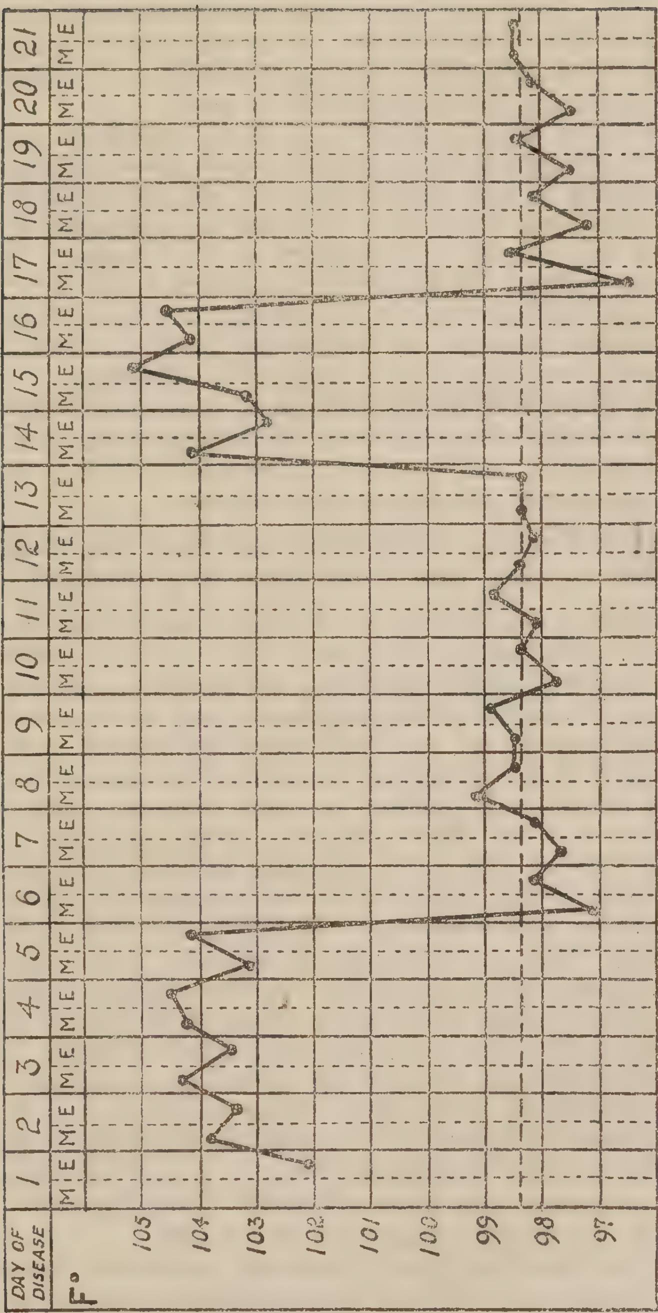
Relapsing fever comprises two main types, louse-borne and tick-borne. Intermediate between these we may place the Spanish variety which appears to be maintained by ticks, but spread in epidemic form by lice.

Various names have been given to the causal organisms of relapsing fever found in different parts of the world :—*Spirochæta* (=*Treponema*) *recurrentis* (European type) ; *S. carteri* (Indian type) ; *S. duttoni* (African type) ; *S. berberum* (Egyptian type) ; but it is probable that these are but varieties of the same species, *S. recurrentis*, and many authorities only recognize this one species (Plate 27).

Both the head and body louse are effective transmitting hosts. Infection is conveyed by crushing the insect on the skin or mucosa. Buxton remarks that the common practice of "popping" lice between the thumb nails may be dangerous on this account. Experiments by Rocha-Lima show the possibility of infection being caused by the bite also. After an infective feed the spirochætes vanish from the alimentary canal of the louse, and reappear later in the hæmocele, the "blood bath" which surrounds the gut and in which it is suspended, and which corresponds to the cœlom in mammals. Infectivity is greatest just before the reappearance of spirochætes in the louse, and is at its height usually about the sixth day after infection. At first the returned spirochætes are small and, according to Nicolle, when they have regained their normal size the louse is non-infective.

Some state that bed-bugs also play a part in the transmission of the disease, but the evidence regarding them is doubtful. It is

Fig. 62.



Typical Chart of European Relapsing Fever.

possible that they are occasionally operative, but, if so, merely act as direct vectors.

Central African relapsing fever is carried by a tick, *Ornithodorus moubata*, and *O. savignyi* is also capable of spreading the disease (*see* page 27). This tick fever was doubtless more common in the late war than the records show, for many cases were mistaken for malaria by those unfamiliar with the malady. It is here described separately from the other relapsing fevers.

Argas persicus and *O. lahorensis* have been held responsible for the spread of relapsing fever in Persia and elsewhere, and epidemiological evidence is adduced in support of the indictment; but, as Nuttall points out, there is at present no scientific evidence that these ticks are capable of conveying the disease. Attempts by Sergent, and others, to transmit relapsing fever by means of *A. persicus* were unsuccessful. *O. talaje* and *O. venezuelensis* have been proved effective vectors of relapsing fever in America, and in Spain *O. morocanus* acts as a reservoir of infection.

Although there are slight differences between European, North African and Indian relapsing fever the diseases are, for all practical purposes, identical, and as the treatment for each is the same the European form only will be described here.

Incubation Period.—This is usually from five to ten days, but would appear to vary from a few hours to a fortnight.

Symptoms.—The onset is very characteristic, being remarkably sudden. The patient is taken with a chill or definite rigor, he feels giddy, an important symptom, he develops a bad frontal headache, pain in the back, joints and limbs, and he may and often does vomit. Implication of the calf muscles, which are often very tender, causes a difficulty in walking. Occasionally convulsions herald the attack. A feeling of heat follows. His temperature shoots up to 104° or 106° (Fig. 62) and his pulse grows rapid, running at 110 or 120. He becomes seriously ill and is quickly prostrated and often delirious. His tongue is moist but coated with a white or yellowish fur. It is to be noted that, in contradistinction to what is met with in typhus, the tongue continues moist throughout the illness save in very grave infections. The patient is constipated, his skin is usually dry, and jaundice may appear, though it is often a mere conjunctival tinge. Thirst, restlessness and vomiting, it may be of blood, complete the picture, but in a minority of cases there is an evanescent rash, either rose spots like those of typhoid or a reddish mottling. Hæmorrhagic forms of the disease sometimes occur. Liver and spleen enlarge. The urine is scanty and high-coloured. The appetite is poor, but occasionally a voracious hunger is developed.

The patient may pass into a toxæmic state with tympanites and hiccup and eventually die, but usually after five or six days of fever the first crisis takes place and is accompanied by profuse sweating and sometimes by diarrhœa. The fall of temperature, often to subnormal, is both marked and sudden. There may be a descent of 10° F. in twenty-four hours. The change in the patient's condition is remarkable. His appetite returns and after a day or two he may feel so well that he is keen to get out of bed. In debilitated

patients, however, the fall of temperature may be accompanied by serious collapse. After a week or so of apyrexia the first relapse occurs. Once again the temperature swings up and all the symptoms of the first stage are repeated, sometimes in a minor degree. Sweating, however, is usually more in evidence and the amount of urine passed is increased.

The temperature remains elevated for three or four days and then a second crisis occurs. The patient may thereafter become convalescent or he may have a second and even a third or fourth relapse, but this is rare in the European form of relapsing fever.

In protracted cases convalescence is slow, but as a rule it is fairly rapid and recovery is complete.

Complications.—Jaundice, severe diarrhœa, epistaxis, hæmatemesis and hæmaturia, parotitis, herpes labialis, pneumonia, meningeal irritation and ophthalmia may be mentioned.

Epidemics vary greatly in intensity. In time of war, amongst starved and debilitated communities, relapsing fever tends to be a serious disease, and the mortality, usually slight, may be very considerable.

Diagnosis.—The spirochæte is found in the peripheral blood during the paroxysms, and can be stained by the Leishman or Giemsa stains, by carbol-fuchsin or by alcoholic gentian violet. It is best demonstrated by the dark-field method either in wet preparations or dry stained films, but with a little care and practice can be detected in an ordinary cover-glass preparation, especially if a 1/12th oil-immersion lens is used, and the film is thin and well spread. Vital staining may be employed, preferably with toluidin blue, a solution of 0·05 per cent. being the best strength. The "thick drop" method with dehæmoglobinization is also useful.

Differential Diagnosis.—At the outset the disease may be mistaken for typhoid, typhus, trench fever, or cerebro-spinal fever, but the peculiar course of the temperature is characteristic and the discovery of the parasite in the blood renders the diagnosis certain. Still it is worthy of mention that an outbreak at Salonika closely resembled cerebro-spinal fever; stiffness of the neck and hyperæsthesia being prominent symptoms. Occasionally relapsing fever may simulate plague, and the two diseases may co-exist. This is also true of relapsing fever and typhus, and of relapsing fever and paratyphoid C. The pains of relapsing fever may cause it to be mistaken for acute rheumatism. The disease is also apt to be confounded with malaria, and malarial attacks may follow relapsing fever and thereby simulate relapses.

Prophylaxis.—The disease being lice-borne, this is the same as for typhus fever. Remember that the spirochæte has been found in the sweat and in the tears, and that it has been proved capable of passing through intact mucous membranes and the unbroken skin. A case is on record where the disease was acquired from infected blood accidentally squirted upon the face.

As bed-bugs may occasionally play a part in the spread of the disease, measures should be directed against them as well as against lice. These will be found detailed on p. 19.

Treatment.—Nursing, diet and general hygienic measures as in typhus. After the crisis the patient is often ravenously hungry; and, if so, it is important to regulate his diet carefully, as injudicious feeding is apt to bring on bad diarrhœa and even dysenteric symptoms.

Happily we now possess specifics in the arsphenamine series. Neoarsphenamine is the most effective preparation and is given intravenously in doses of from 0·3 g. In the Egyptian form 0·6 g. doses have often been found necessary. One full dose as a rule suffices, but the drug should never be given if the duration of the attack indicates the crisis to be imminent, nor in any apyrexial period. If relapse occurs the injection should be repeated as the temperature rises. Sometimes an injection produces a temporary aggravation of the symptoms, but the curative action is usually rapid and certain. Albuminuria is not a contra-indication. Galyl has been found effective in doses of from 0·3 g. to 0·4 g., and other arsphenamine substitutes may be employed in corresponding doses. Sulphoxyl-salvarsan has been well reported on in doses of from 0·3 g. to 0·6 g. This last-mentioned preparation can be given intramuscularly.

In debilitated persons camphor, ammonia, digitalis and stimulants may be indicated. Sometimes the back and limb pains demand the exhibition of opium. If hiccup is troublesome, blistering over the line of the vagus on the left side of the neck may be tried.

Central African Form (Tick Fever)

Etiology.—The causative spirochæte *S. duttoni* is morphologically indistinguishable from the other so-called species mentioned already.

The chief vector is the tick *Ornithodorus moubata* (Plate 2), one of the Argasidæ, concerning which details will be found in the section "Arthropod Pests." It suffices here to say that it was present in many parts of East Africa in 1914–18, that its habits rather resemble those of the bed-bug, that it bites at night, both male and female being blood-suckers, that it lives in huts, bandas, rest-houses and under the shade of trees where the soil is dry, and that it may be carried long distances in packs and blankets. Its bite may sometimes be followed by some local inflammatory reaction, but often passes unnoticed. Infection takes place as a result of its infected fæces contaminating the tick-bite. One tick can infect.

Symptoms.—Generally speaking, these resemble those of the European form and need not be recapitulated, but certain differences should be noted. The initial fever is generally shorter and may terminate within three days (Fig. 63). Frontal headache and pains in the bloodshot eyes are rather characteristic. Diarrhœa not infrequently occurs and there may be dysenteric symptoms. The apyretic intervals vary greatly in length. They tend to become longer later in the disease if, as may be the case, many relapses take place. As many as eleven have been noted. The spleen is usually enlarged and tender, but the liver dullness is not as a rule increased. The blood shows a leucocytosis.

The attack is very debilitating, especially in Europeans.

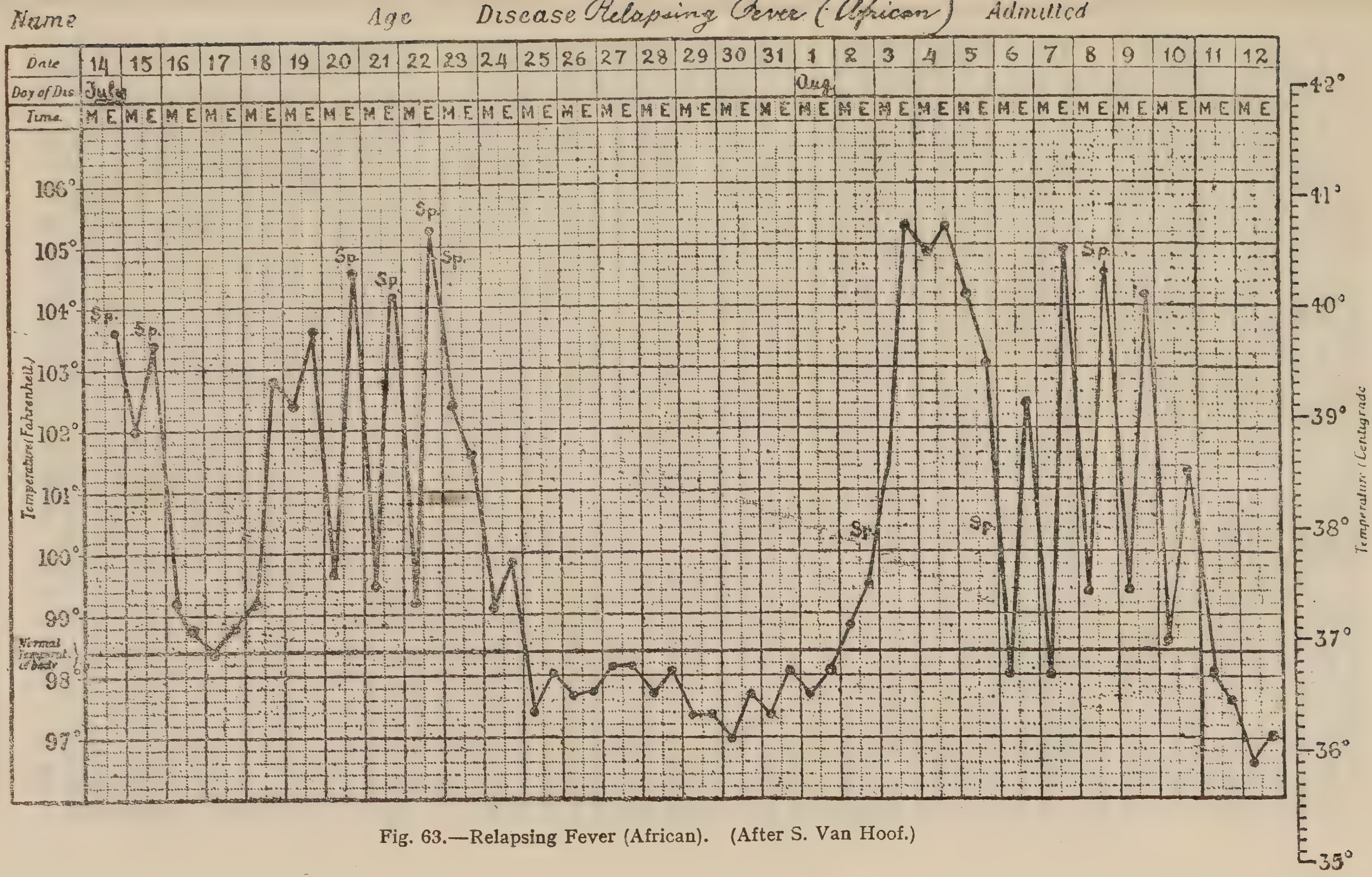


Fig. 63.—Relapsing Fever (African). (After S. Van Hoof.)

Complications.—Affections of the nervous system are not uncommon, including meningeal reactions with a pleocytosis, and paresis involving the 6th and 7th cranial nerves. Inflammatory conditions of the eye, such as iritis and iridocyclitis, may also develop. When the disease runs a long course myocarditis may become an important feature.

Diagnosis.—This can only be made with certainty by finding the spirochæte in the blood. The thick-drop method should always be tried as, apart from dark-field scrutiny, it is most likely to yield positive results. Spirochætes are very scanty in the tick-borne variety.

Differential Diagnosis.—In East Africa during the last war the disease was usually confounded with malaria, but it may be confused with cerebro-spinal fever and plague.

Prophylaxis.—Avoid the neighbourhood of native huts and of rest-houses. Native bedsteads of wood with string or hide are dangerous. If used their legs should be smoothed to prevent ticks climbing up them. It is best to employ a hammock. Sleeping on the ground favours infection. A mosquito net is useful, as it prevents the access of ticks during the night. Bandas should be constructed in such a way as to lessen the chances of tick infestation. For example, the reed walls of huts and bandas should be so constructed as not to reach the ground, so that a space of eight to ten inches will intervene between the latter and the bottom of the walls. Mud and rubble buildings are inadmissible. Floors should always be raised six or eight inches and, if not cement, beaten hard and kept clean. A trench with perpendicular sides dug round a banda or hospital ward and filled with wood ash has been found useful in keeping wandering ticks away. The use of a night-light is recommended.

Camps should be placed as far distant as possible from native villages and from buildings known to harbour tick vectors. Periodical inspections of packs and blankets should be held. Temporary infected buildings in lines and camps are best burned down. The ground can be fired *in situ* or the floors dug up to a depth of several inches, removed and pitted or treated with fire, care being taken that ticks do not migrate during the process. In permanent buildings fumigation with pyrethrum powder may be employed.

Treatment.—That recommended for other forms of relapsing fever frequently fails in tick fever. Neoarsphenamine in 0·9 gramme doses appears to give the best results. It should be injected at the first attack of fever ; failing this, wait until the first relapse and give it when the temperature rises. Never administer the drug during the apyrexial period. If this fails, Mercurochrome intravenously (20 c.cm. of a 1 per cent. solution) may be tried. Stovarsol has been claimed to be effective in doses amounting to 24 grains in the day, given by the mouth. A dose as large as this is, however, not recommended.

Owing to the poor response to arsenicals and other preparations in tick fever, some observers limit themselves to symptomatic treatment and administer digitalis or strophanthus to aid the heart.

On account of the nature and habits of its vector (*Ornithodorus moubata*), African tick fever is a sporadic "house" or "place" disease in contrast to epidemic louse-borne fever. In both cases, as far as is known, man constitutes the sole reservoir of infection.

Other Tick-borne Relapsing Fevers

These are found chiefly in two large areas. The first is chiefly limited to districts bordering on the Mediterranean, where it occurs along the North African Coast, Southern Spain, and over an extensive area extending eastwards to Persia, Turkey, and Transcaucasia. The second embraces the greater part of Southern America, including many of the Southern States of the U.S.A.; Central America; and the northern part of South America.

The vector is varying species of *Ornithodorus*:—*O. savignyi*; *O. talaje*; *O. hermsi*; *O. wheeleri*; *O. turicata*; etc.

The infecting organism is a spirochæte, apparently identical with *S. recurrentis*, and which has, as mentioned above, been given a variety of names in the countries in which it occurs. These varieties of tick-borne fever differ from the classical epidemic form and also from East African tick fever in that a number of small rodents (rats, squirrels, etc.) and some larger animals (dogs, American monkeys) have been incriminated as animal reservoirs of infection.

The tick transmitters do not normally parasitize man and are found in the burrows of infected rodents. In consequence, the infection in man is considered an accidental occurrence and transmission from man to man is relatively rare.

RICKETTSIAL INFECTIONS OF MAN

Rickettsiæ are minute diplococcal or rod-like bodies which can be demonstrated when suitably stained by Giemsa's fluid and examined microscopically. Generally they are smaller than bacteria—less than 1 μ. in the longest diameter—but they exhibit considerable pleomorphism and larger and thicker forms or even chains may be seen.

Characteristically the rickettsiæ infecting man cannot be cultivated on ordinary culture media and only develop in living tissue, tissue cultures or in the presence of fresh tissue. Normally they develop in the alimentary tract of certain blood-sucking arthropods. In the case of exanthematic typhus the rickettsiæ are taken into the louse with the blood feed, where they develop in the alimentary canal. Infective rickettsiæ not only pass out with the fæces, but also invade the intestinal epithelium and eventually cause the death of the insect. Other rickettsiæ appear to be harmless to their arthropod hosts.

When man or a susceptible animal is infected, either naturally or experimentally, with the fæces of arthropods containing certain types of rickettsiæ, the rickettsiæ invade and develop in their tissues, giving rise to various clinical conditions. Not all rickettsiæ, however, are infective to man.

Man is susceptible to a number of rickettsial infections, the most important of which are exanthematic or epidemic typhus, murine or endemic typhus, and Tsutsugamushi or rural typhus of the Far East. The table below gives certain information regarding these diseases to which reference is made later

Disease	Weil-Felix Reaction	Geographical Distribution	Insect Vectors	Possible Vertebrate Reservoirs
Exanthematic typhus.	OX19++++ OXK−	Europe, Abyssinia, North Africa, Belgian Congo, Asia Minor, Persia, North China, Mexico.	Louse, *Pediculus humanus.*	Man.
Endemic or murine typhus.	OX 19+++ OXK−	World-wide.	Rat flea, *Xenopsylla cheopis.*	Rat (squirrel, shrew).
Tsutsugamushi disease (scrub or rural typhus of Far East and hill typhus of India).	OX19− XK+++	Japan, Formosa, Malaya, Java, Sumatra, New Guinea, India, Burma, etc.	Larva of— *Trombicula akamushi* (Japan), *T. deliensis* (Malaya), *T. deliensis* (India), *T. minor* (New Guinea).	Bandicoot, field mice.
Rocky Mountain spotted fever (Eastern and Western forms).	OX19++ OXK++	U.S.A.	*Dermacentor andersoni, D. variabilis.*	Goats, hares and other small rodents.
Fièvre boutonneuse.	OK19++ OXK++	Mediterranean Zone.	Dog tick, *Rhipicephalus sanguineus.*	Dog.
South African tick typhus.	OX19++ OXK++ (Tick-borne typhus also occurs in Abyssinia and in Kenya, where the dog tick *Rhipicephalus sanguineus* acts as vector).	South Africa.	Ticks, *Hæmaphysalis leachi.*	Dog ?
Sao Paulo rural typhus.	OX19++ OXK++	Southern Brazil.	Tick, *Amblyomma cajennense.*	Opossum.
Q fever.	OX19− OXK−	Australia, U.S.A.	Ticks, *Hæmaphysalis humerosa, Dermacentor andersoni, D. occidentalis, Amblyomma americanum, Rhipicephalus sanguineus ?*	Bandicoot.
Trench fever.	OX19− OXK−	North Africa.	Louse, *P. humanus.*	Man.

TYPHUS GROUP OF FEVERS

Exanthematic Typhus.—Exanthematic or epidemic typhus has been one of the scourges of armies since prehistoric times, and it remains a menace to-day whenever the vicissitudes of military service prevent the efficient cleansing of the person and clothing. Infestation of armies with lice can only be controlled when conditions are favourable ; it cannot be absolutely eradicated. When the means for adequate cleansing of the body and the clothing do not exist the infestation, both rate and degree, will rise again.

Etiology.—It is generally accepted that the appearance of exanthematic typhus in a community is due to the previous existence in that community of endemic or murine typhus and the infestation of its members with lice.

Murine typhus is transmitted from the rat to man by the flea *Xenopsylla cheopis.* It does not occur epidemically, and although the symptoms and pathology are essentially the same as those of exanthematic typhus it is a comparatively mild disease. When, however, sufferers from murine typhus are lice-ridden these arthropods become infected when they feed on such patients. The fæces of such lice are infective to man, and although in the early stages of this "passage" the rickettsiæ appear to retain their murine characters, yet after a few "passages" through the louse-man cycle they appear to take on exanthematic properties and the disease becomes epidemic.

The infection is conveyed by lice, and it is probable that they constitute the only means of spread. Both varieties of *Pediculus humanus* are effective vectors of the disease. Infection takes place through cutaneous lesions into which the infected excrement of the insect has been scratched or rubbed. It is possible that infection may also be conveyed by the powdered infective fæces becoming suspended in the air and attacking the mucous membranes of the upper respiratory passages.

The causal organism is a form of *Rickettsia* to which the name *R. prowazeki* has been given.

"Lice which have sucked blood containing the virus are capable of producing infection during seven to eleven days after they have infected themselves. If such lice are crushed nine to ten days after an infective feed, or if their fæces are collected three to six days after they have fed on infective blood, their contents and fæces respectively are capable of producing infection if placed upon the excoriated skin" (Nuttall). The duration of infectivity in the louse is unknown.

Pathology.—Exanthematic typhus is a disease of the smaller blood vessels. The lesions are located chiefly in the endothelium lining the blood vessels of the skin, central nervous system and skeletal muscles. They may be demonstrated to a less extent in those of the viscera, heart, kidney and testes. The reaction to the rickettsiæ is a degenerative change giving rise to thrombosis. There is also a proliferative reaction on the part of the vascular endothelium giving rise to the characteristic microscopic nodules in the skin and central nervous system. Death from typhus is frequently the direct result of extensive proliferative reaction in the brain.

Incubation Period.—This varies between five and fourteen days, twelve days being the usual time.

Symptoms.—These vary in different outbreaks, and an attempt has been made to present a composite picture of the disease.

The onset may be slight, there being only the discomfort of a mild headache, pain in the back together with a loss of appetite; or it may be sudden and well marked, and the patient, in addition to the above symptoms, suffers from cold shivers, the eyeballs are tender on pressure and there is a sense of lassitude, malaise, and faintness. Occasionally general convulsions passing into delirium herald the attack. The period of onset lasts about two days, and on the third day the symptoms become aggravated and the true signs of typhus begin to make their appearance. The patient,

though he may be going about, has a flushed face and congested eyes. The facies has been described as what might be seen if one could imagine a bad cold in the head without catarrh, *i.e.* with the secretions suppressed instead of excessive and the tumidity absent. The pulse rate increases while the temperature may still be normal—an important point in early diagnosis. Two other helpful early signs are bands of injection on the conjunctivæ, extending from either canthus to the cornea, and slight contraction of the pupil, a sign much stressed by the old physicians, at any rate in Ireland.

Epistaxis is frequent in some epidemics and may be profuse and persistent. There is a general reddening of the skin and what has been termed a "watercourse" appearance is not uncommon, red channels running here and there and combining to form erythematous patches. The conjunctivæ may become congested and some nasal obstruction, with slight discharge from the nose, may manifest itself. There is no splenomegaly at this stage.

On the second or third day the temperature begins to rise and after a morning remission runs up to 103° to 104°. Its usual course is shown in the charts, the fall being by lysis (Fig. 64). There may be preconvalescent rise.

Cases with remittent temperatures are encountered, and these are said to do badly owing to cardiac trouble. The urine is normal. The rash generally appears on the fifth day, being found first on the upper part of the abdomen and spreading thence to the chest and shoulders. The face remains unaffected. The eruption often extends all over the body except the face, but it is more profuse on the trunk, especially on the back. The rash tends to be polymorphic. In a Galician outbreak the following types were in evidence :—

1. Generalized exanthem on the body.
   (*a*) Small macular type, with eruptions of uniform-size.
   (*b*) Large macular type, with various different-sized eruptions.
2. Petechial exanthem.
3. Eruption especially developed on the elbow and upper arm, but similar to that on the trunk.
4. Localized on the palms of the hands and soles of the feet, with various clinical forms.
5. Very early-formed small petechiæ in pre-existing growths.

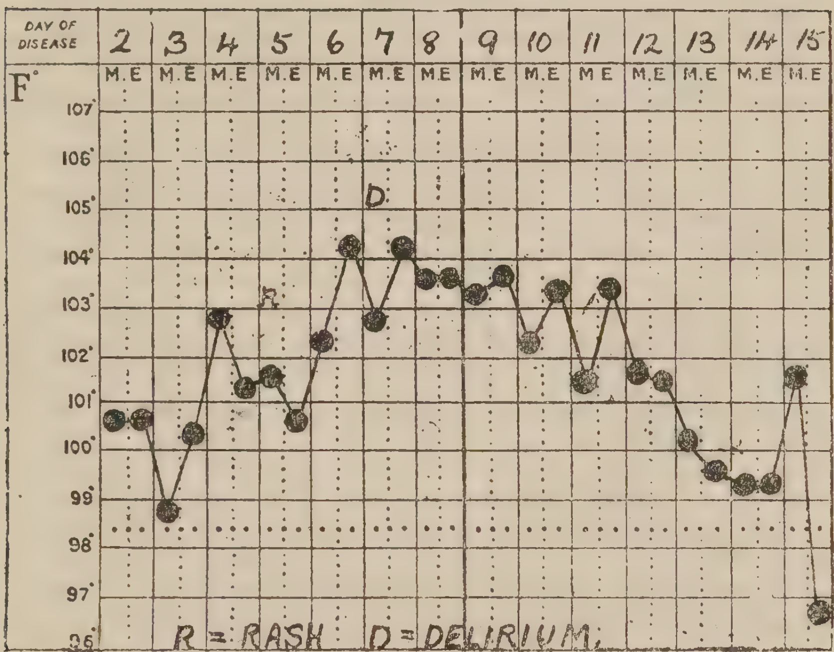
The "mulberry" aspect is by no means always present, nor indeed, is a definite spotted rash. The "watercourse" appearance may persist and there may be an erythema. At the same time, the three elements of the "mulberry" can usually be distinguished, namely, the rose-pink spots fading to a dirty brown or coppery hue, the subcuticular mottling and the petechiæ. The spots persist for five to ten days.

Along with the rash there is a buccal erythema, and red spots may be seen on the palatal mucous membrane.

As the rash develops the patient begins to look seriously ill. The headache grows more intense, and he sinks into the typhus state, becoming dull and lethargic, with sluggish movements and a foul mouth. What with his bloated face and congested skin and eyes,

he looks as though he were drunk. He is difficult to rouse, and lies on his back with a vacant stare on his flushed face and, it may be, a tendency to squint; his voice is husky, his hands are tremulous, and he is somewhat deaf. His cerebration is slow, he is very thirsty, he can scarcely show his dry, brown tongue, and there may be detected the curious and characteristic typhus smell aptly described as being like a cupboard full of well-blacked boots. There is a certain " tang " in it to which the above simile does justice. The breathing is rapid, and there is usually some bronchial catarrh with cough and thin expectoration. In the second week coma, low muttering delirium, and retention of urine appear in all but the milder cases. At this stage the urine may contain albumin and casts, and the spleen will be found somewhat enlarged. The patient

Fig. 64.



Temperature Chart of a Case of Typhus Fever ending in Recovery.

becomes more and more like a log. He is constipated, often wets the bed, and shows signs of cortical irritation such as twitching and hyperæsthesia.

If he is going to recover, a change for the better sets in about the fourteenth day; his mind clears, and within a week he is hungry and convalescent though weak and flabby. If he is going to die the coma deepens, his tongue continues dry and crusted, the temperature remains elevated or rises and the heart fails (Fig. 65). Sometimes a patient will die after the crisis from exhaustion or complications. There is some evidence to show that the virus remains in the body for three weeks after the fever abates.

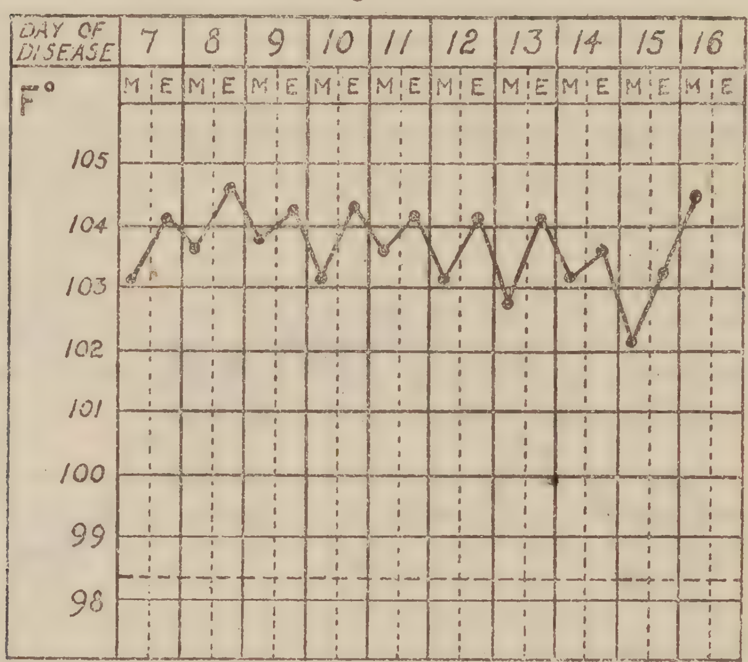
While the above description is that of a more or less typical case of typhus, it must be remembered that there are mild cases without

much nervous upset or prostration, cases almost or wholly devoid of a rash, fulminant cases with early and violent delirium which succumb quickly, and what has been called the "high-tension type," with very severe headache and photophobia lasting throughout the entire pyrexia period, no delirium but mental irritability. The pulse is relatively slow but very full and bounding.

As regards the blood in typhus, there would seem to be a leucocytosis during the febrile period. In grave cases there is a reduction in the number of polymorphs and an increase in the large mononuclears. The eosinophiles are markedly diminished.

The cerebro-spinal fluid is said to exhibit a marked leucocytosis.

Fig. 65.



Temperature Chart from the seventh day of a Case of Fatal Typhus Fever.

Complications.—Hypostatic congestion of the lungs, myocarditis, venous thrombosis, otitis media, parotitis, bed sores and gangrene of the feet may be mentioned. Diarrhœa is sometimes so profuse as to require treatment. The disease may be followed by peripheral neuritis and distressing neuralgias, but the convalescence is usually rapid and complete.

Prognosis.—The prognosis in the young adult who is reasonably well fed is very fair, but in those debilitated by famine and those over the age of forty years the outlook is uncertain. Those who develop early delirium are very apt to die.

Diagnosis.—As an aid to diagnosis the production of artificial stasis of the vessels is said to be useful. Where the rash is not characteristic or is sparingly developed place a bandage round the arm. The resulting engorgement of vessels shows up the exanthem

more clearly, and the red maculæ can be observed to take on a blue, cyanotic hue, which eventually changes to the brown or coppery colour already mentioned.

Short of the recovery of the infecting rickettsiæ or the demonstration of the rickettsicidal antibodies in the serum of patients the Weil-Felix reaction is the most certain method of diagnosis. It is the only routine laboratory test that is employed at the present time. The reaction depends on the fact that sera of individuals infected with the rickettsiæ of the typhus group of fevers contain antibodies that react with certain strains of Proteus organisms.

The true nature of the reaction is still imperfectly understood, but although the sera of typhus patients may agglutinate a variety of Proteus strains, the so-called specificity of the reaction is restricted to the interaction of the O-antigen of certain X strains and th O-antibody in the sera. The more important strains concerned ar the O-variants known as Proteus OX19 and OXK. Suspension of Proteus OX2 are also employed by many workers. The strain OX2 is more closely related to OX19 than to OXK, and for the sake of clarity the Weil–Felix reactions in different rickettsioses in the table have been limited to the strains OX19 and OXK. As will be seen from this table the sera of patients suffering from exanthematic typhus agglutinate suspensions of Proteus OX19 only.

The agglutinins may be detected as early as the fourth day in certain cases of exanthematic typhus, but usually are not appreciable until a day or two later and may even be delayed until after the tenth day.

The maximum titre developed during the disease is very variable and although there is generally a rough correlation between the severity of the illness and the maximum titre, non-reacting cases—usually ending fatally—may be observed on rare occasions. The titre may rise to as high as 1–100,000, but the usual range is between 1–1,000 and 1–5,000.

The sera of normal individuals may agglutinate suspensions of both OX19 and OXK in low dilutions, and such agglutination is more frequently observed in the case of OXK suspensions. Any reaction with a serum diluted 1–100 or more, however, must be regarded as very suggestive. But the most important criterion is the rapidly rising agglutinin titre as the disease develops.

The sera of individuals suffering from diseases other than typhus may agglutinate O suspensions of Proteus X. Chronic brucellosis, toxoplasma in adults, tularæmia, typhoid fever in inoculated subjects are the chief examples. Although there may be early and appreciable titres with OX suspensions, it is very rare to find any significant rise in titre as these diseases develop.

Conversely the sera of patients suffering from typhus may agglutinate suspensions of brucella and typhoid organisms. Here, also, there is little to confuse diagnosis as there is no significant rise in agglutinins when serial estimations are undertaken during the course of the disease ; the titre with the particular proteus suspension steadily increases, whilst the titres with the other antigens do not show any significant increase. It may be of interest to note that in the case of *Bact. typhosum* suspensions early and appreciable titres with the H, O and Vi antigens may be observed.

Differential Diagnosis.—Typhus has specially to be distinguished from typhoid and paratyphoid, while it may also be mistaken for lobar pneumonia, influenza, cerebro-spinal fever, measles, relapsing fever (may be also lice-borne), plague and septicæmia.

Treatment.—Although the sufferer from exanthematic typhus requires good nursing at the earliest opportunity, the first step in treatment is the prevention of spread of the infection from the patient. This consists of the removal and destruction of all lice and nits from the patient's body and clothing before admission to the hospital ward. These procedures should be undertaken in a special reception room, suitably heated, on the floor of which is spread a large sheet. The clothing is removed from the patient with great care so that the lice or their fæces are not scattered. They are laid in the centre of the sheet together with any blankets or bedding brought with the patient and tied into a bundle. If immediate disinfestation is not possible the bundle should be immersed in 2½ per cent. cresol for one hour. Immediately the clothing has been removed, the patient should be placed on other clean sheets, the hairy parts of the body and head rapidly smeared with soft soap or a soft germicidal ointment to smother the remaining lice and their fæces. The body is well washed, every hairy part shaved and the hair of the head cut short with fine clippers. The attendants carrying out this work should wear special protective clothing, including a closely fitting cap to cover the head completely. Goggles and masks may also be advisable.

The patient's body is then carefully inspected for any remaining lice, special care being paid to the perineal and anal regions. If the inspection is satisfactory the patient may then be wrapped in clean blankets and taken to the ward by fresh attendants without fear of spreading the infection.

There is only a small chance of patients suffering from exanthematic typhus being infective to other patients or to nursing attendants if they have been freed from lice and their nits, and if re-infestation is prevented. Droplet infection is nevertheless a possibility.

The most important aspect in the actual treatment is skilled and disciplined nursing. The early delirium or maniacal symptoms that may develop call for special attention and care.

The use of hyperimmune serum in doses of 20 c.cm. is likely to be beneficial in toxic cases if administered early in the disease. The supply of the serum is, however, extremely limited, and it is unlikely that it will be generally available. Apart from this there is no form of specific therapy and treatment is essentially symptomatic. Sedatives are nearly always required and of these preparations containing morphia are, on the whole, the most successful. Strophanthin is the drug of choice for a cardiac stimulant. Lumbar puncture, withdrawing about 30 c.cm. of cerebro-spinal fluid, is beneficial in relieving cerebral symptoms and this procedure may be repeated if necessary.

Prophylaxis.—The prevention of exanthematic typhus in any community where endemic typhus exists is dependent on the prevention of louse infestation or the development of complete

immunity to the disease. At the present time it is extremely doubtful whether either of these are feasible.

Under favourable conditions, where bathing and disinfestation facilities exist, it is possible to so control louse infestation as to make the spread of exanthematic typhus unlikely. The success of such measures is dependent on the continuous and efficient working of the machinery of the hygiene organization. Unless each individual member of the community can be bathed and issued with clean clothing once a week infestation will return.

Insecticides, such as derris root compounds (A.L.63) and lauryl thiocyanate may be most usefully employed as adjuncts to other methods of disinfestation. Small-scale trials of these preparations have been promising, but until extensive field trials under adverse conditions have been completed their full value cannot be assessed.

There are several varieties of rickettsial vaccines for immunization against exanthematic typhus, but they now are all essentially killed suspensions of rickettsiæ from cases of this disease.

The type at present considered to be the most promising is prepared by cultivating the rickettsiæ in the yolk sac of the young developing hen's egg. None of these vaccines have been shown to induce immunity, but there is evidence that serial inoculations of killed suspensions of rickettsiæ cultivated by the yolk-sac method afford a relative protection which, if it will not prevent the development of the disease, will at least reduce the severity of the symptoms. At present, however, there is insufficient evidence to express any definite opinion as to the true value of these vaccines.

In dealing with any outbreak of exanthematic typhus, medical officers, nurses and hospital attendants are obviously exposed to greater risks than the rest of the community and in past epidemics this group of individuals has suffered greatly from the disease ; yet they can be most ill-spared under such conditions. Whether or not mass immunization is adopted, it is recommended that all medical personnel should be fully inoculated with the most efficient typhus vaccine available.

Other Fevers belonging to the Typhus Group

Other members of the group are named in the first part of table on p. 218. It will be seen that with the exception of murine typhus, which is world wide in its distribution, these conditions are restricted to certain territories and that generally their incidence is seasonal according to the insect vector. The table in question is by no means complete for there is little doubt that many fevers, now called P.U.O. in the absence of an exact diagnosis, occurring in tropical and subtropical areas belong to this group of diseases.

The clinical picture and pathology of the group are essentially those of the principal member, exanthematic typhus, but generally the symptoms are less severe.

Rocky Mountain Spotted Fever is, however, usually a severe disease and may have a high mortality. It is spread by the bite of a tick, but is generally unassociated with a local lesion. The distribution of the rash differs from that of the group inasmuch as it appears on the palms of the hands and the soles of the feet.

Tsutsugamushi disease is spread by the bite of a larval mite. In the Far East the bite frequently results in the formation of a local ulcer with lymphangitis and adenitis. The maculo-papular rash usually commences on the face and then spreads to the limbs and trunk, but does not become petechial. In India a closely associated condition is not uncommon in the hills, but there the local lesion is not evident and the rash may be very slight or even absent.

The mild typhus-like Q fever of Australia and the U.S.A. fails to produce anti-bodies in the blood that react with any O-antigens of proteus X bacilli that are at present known.

TRENCH FEVER

This condition, apparently a distinct and hitherto unrecognized disease, was first reported amongst the troops in France in the war of 1914–1918, but occurred in the Salonika area and seemingly also in Egypt. There is evidence to show that it was introduced into the Mediterranean area from France. There is no record of its occurrence in East Africa, but it was reported from Mesopotamia.

Although trench fever apparently disappeared as a clinical entity soon after the last war and has not yet returned, two localized institutional outbreaks of a similar fever, in both instances associated with lice infected by a member of the *Rickettsia* group of organisms (*R. weigl*) have been reported from Poland, the last outbreak occurring in 1939. Whether this fever, known as Weigl's disease, is identical with trench fever is unknown. A disease resembling trench fever is still endemic in Tunis and is caused by rickettsiæ morphologically similar to *R. quintana*. Cultures of these rickettsiæ inoculated into volunteers have set up an infection clinically resembling trench fever. These rickettsiæ are not pathogenic to rhesus monkeys, mice, rats, rabbits or guinea-pigs.

Etiology.—It is generally accepted that trench fever is due to *Rickettsia quintana*, found in the gut and excreta of infected lice. The louse, *P. humanus*, has definitely been proved to be the vector. The infection is usually derived from the excreta of infected lice scratched or rubbed into skin abrasions.

The fact that it is the excreta which are infective explains cases of trench fever occurring in wounded men who have not harboured lice for long periods, because the dried infected excreta blown on to a raw surface will readily cause the disease. A man may be entirely free from lice at the time he develops trench fever, the louse that infected him having left him some time previously, or he may have contracted the disease from blankets, etc., contaminated with infective louse fæces.

It has been shown by Byam that the virus in louse fæces can resist drying at room temperature, exposure to sunlight, hot water and soap as used in washing clothing by hand, and can withstand keeping for at least four months. The virus is not affected by twenty minutes' exposure to dry heat at 80° C., but moist heat at 50° C. will sterilize it in twenty minutes. So that clothing, etc., although effectively loused, is not necessarily disinfected.

Lice become infective after a period varying from five to eight days from an infecting feed, and probably remain infective for the

remainder of their life. They cannot transmit the virus through the egg to their offspring. Lice have been infected by feeding on a patient on the 443rd day of the disease (Byam).

Incubation Period.—The incubation period of the naturally occurring disease is difficult to estimate with accuracy, but experimental evidence suggests that it is in the region of eight days.

Symptoms.—In considering the symptomatology we are at once confronted with a difficulty, inasmuch as the term Trench Fever, an unsuitable one in any case, has been loosely applied to include not only the true trench fever, which is a definite relapsing fever, but also at least two other febrile conditions, commonly classed as P.U.O., one of an influenza-like type, the other recalling an enterica infection. It is not surprising that this error has been made because, apart from the pyrexia, the symptoms of these three diseases, as pointed out by the British Committee on Trench Fever, are indistinguishable from one another. As the Committee states, "All exhibit similar pains, all produce enlargement of the spleen, none show intestinal or renal symptoms of any importance, and all are apt to produce tachycardia."

Here only the true relapsing trench fever will be considered. Even then there is apt to be confusion, for there are two forms of fever which occur at different stages of the disease.

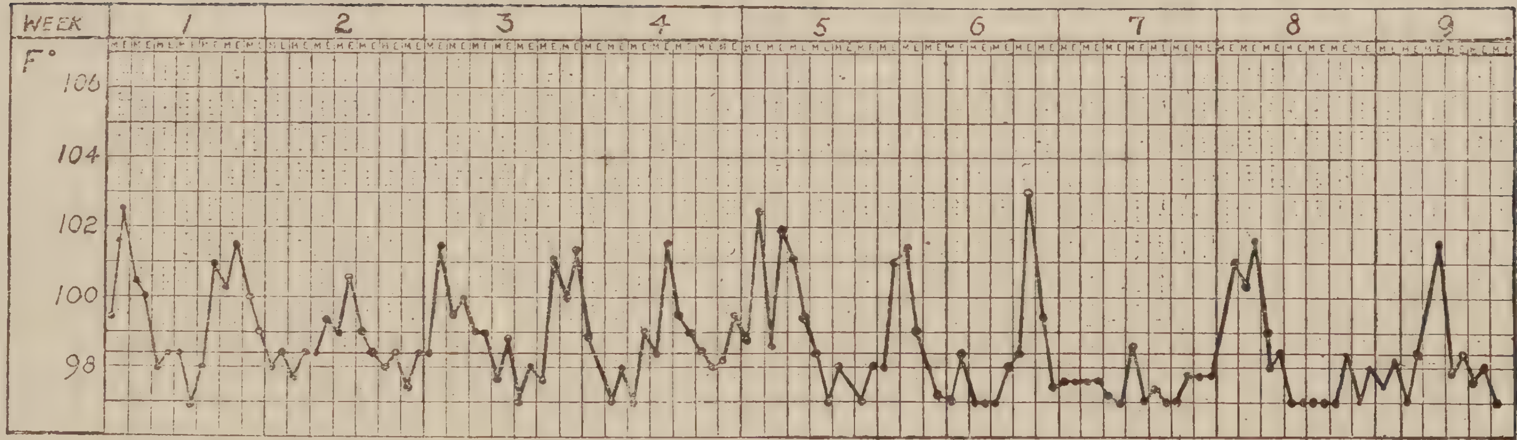
Briefly the symptomatology is as follows:—

Prodromal symptoms rare and unimportant. Onset usually sudden, with headache, dizziness, pain chiefly in the legs and back. It may, however, be generalized, and abdominal pain is not infrequent. Pain behind the eyes, especially when they are moved, is a notable feature.

Attention is usually specially directed to the pain in the limbs, which is always worse at night. It may be of a dull aching, gnawing or boring type, or be acute and lancinating, lasting for many hours. This latter form constitutes the now well-known shin pains, which are felt in the bones and have been attributed to neuralgia of the nerves in the periosteum. The general pains have been attributed to an infectious fibrositis. The pains may shift about, and very often begin about 5 or 6 o'clock in the evening. They may be associated with great superficial tenderness, so that not even the weight of the bedclothes can be borne. Sometimes at the start the weakness of the legs is so great that the patient cannot stand. Alternate shivering and sweating is a peculiar and very constant feature, while some authors describe cases with vomiting and diarrhœa and a rare type presenting, at the onset, cerebro-spinal symptoms. The conjunctivæ are congested, the tongue is dry with a yellow fur down its centre flanked by red margins. There is usually constipation.

The spleen enlarges, and in 70 to 80 per cent. of the cases small erythematous spots or papules make their appearance chiefly on the chest, back and abdomen. They are usually flush with the skin and pink in colour, and disappear on pressure. There may be few or a couple of hundred, and they are often evanescent. Sweating is common, catarrhal symptoms rare, albumin in the urine not infrequent.

Fig. 66.



Trench Fever. (After Byam.

Labial herpes is often seen. The blood shows a leucocytosis and an increase of polymorphs up to 90 per cent. during the febrile periods. The lymphocytes are said to show a slow relative increase during convalescence.

In bad cases the patient becomes anæmic, and owing to lack of sleep, the result of the severe pains, he presents a worn, haggard look, and suffers from mental depression. As a rule, however, the eye remains clear and bright, thus differing from the dull and half-closed eye of the enterica group of fevers.

The pyrexia calls for special mention (Figs. 66 to 70). The two forms already mentioned as occurring at different stages of the disease are in order of sequence :—

1. An irregular remittent and intermittent fever lasting for a period rarely exceeding four weeks. It may be so slight as to escape notice.
2. A definitely intermittent fever, often showing a regular periodicity, and sometimes extending over a period of many weeks.

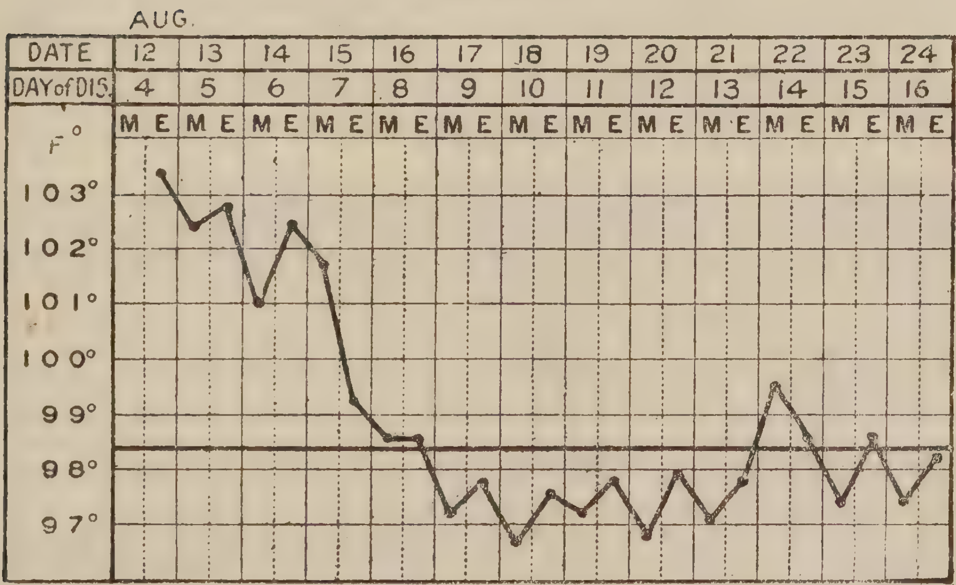
These two together constitute the complete pyrexial wave of the disease, but it is important to note that the first form, when well marked, may present three types of temperature curve :—

(*a*) A short, influenza-like fever wave, lasting about three days.

(*b*) A similar wave followed, usually on the sixth, seventh, and eighth days, by a febrile relapse, the interval being afebrile. Irregular fever may follow.

(*c*) The initial wave may run more or less into the relapse and produce a so-called saddle-back (dengue-like) or pseudo-typhoid temperature. Irregular fever may follow.

Fig. 67.



Trench Fever.

Fig. 68.

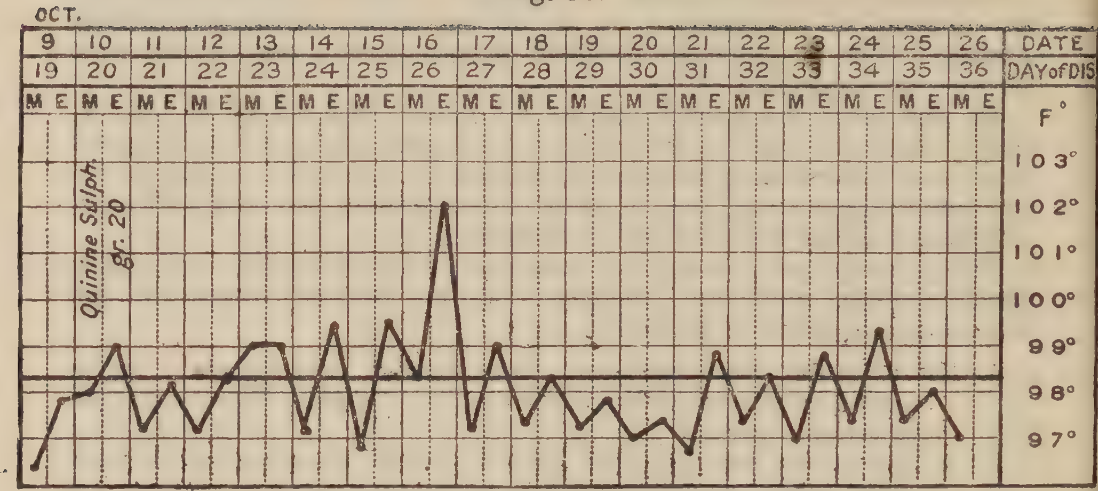


Fig. 69.

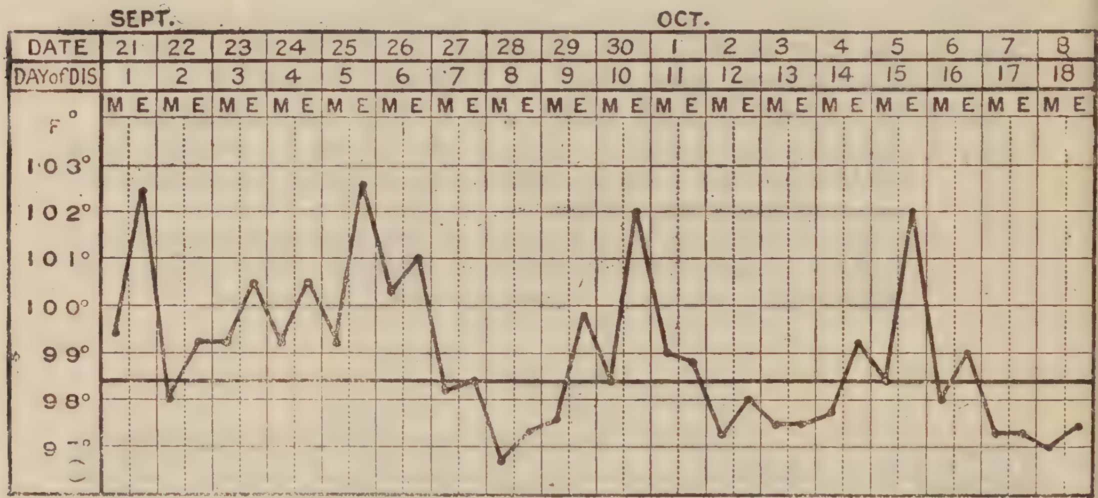
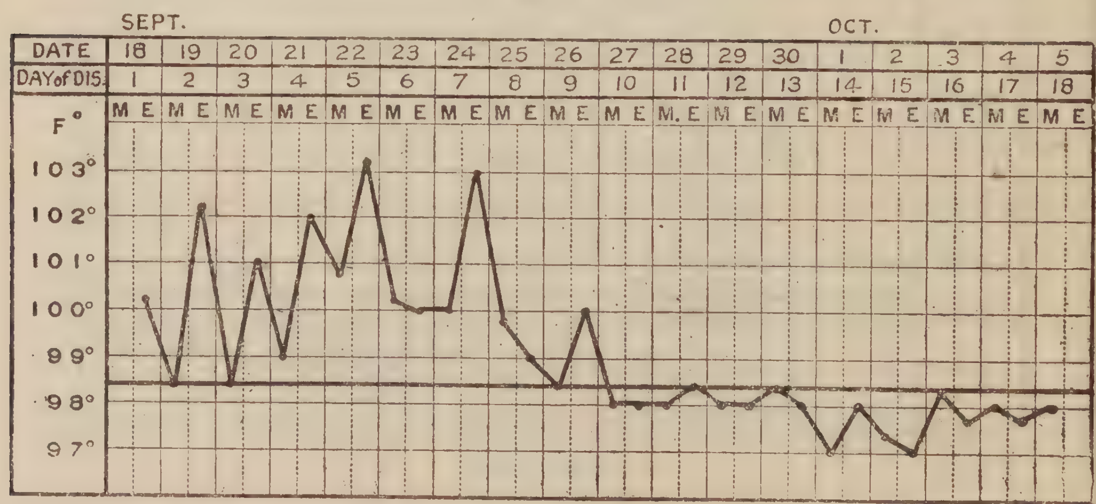


Fig. 70.



Figs. 68–70.—Charts illustrating various types of Temperature in Trench Fever.

The above are the types recognized by the War Office Investigation Committee.

The second form of fever which from its peculiar character led to the recognition of trench fever as a definite clinical entity is, as stated, a continuation of the first form, and only occurs late in the disease. It may follow on immediately after the first form, blending with it as it were, or it may not appear for many months, the disease in the meantime being apparently in quiescence as, in such cases, the chances of reinfection were excluded.

This secondary fever may be merely a single " spike " or a series of " spikes," suggesting the appearances met with in relapsing fever.

The temperature shoots up to about 104° F. In the single " spike " form it falls rapidly and continues on or about the normal line. In the multiple " spike " form the fever recurs at intervals which usually vary in duration, but may be periodic (often four-day periods). The later " spikes " tend to be more irregularly spaced. In the non-febrile periods the temperature is subnormal. The highest temperature is usually reached in the evening, but this is not invariably the case.

While the above appears to be the general course of the disease, it is clear that many irregularities occur. Indeed at least four irregular clinical types have been described, but into these we need not here enter.

The pulse-rate in the early stages is quickened, corresponding to the rise of temperature ; later it tends to be slow in respect to the degree of fever present.

A loss of sensation, varying in degree, has been noted in the middle and later stages of the disease.

Trench fever, though not a fatal malady, is a very crippling one, for it not infrequently leaves behind it a train of unpleasant sequelæ. Of these the most important is disordered action of the heart, or irritable heart, the result of a myocarditis which may produce dilatation or merely a muffling of the first sound. On the other hand, the first sound may be loud with a slapping impulse.

Tachycardia is common, and there is dyspnœa on exertion. Other troubles are anæmia and persistent pain, especially in the shins.

Diagnosis.—Unlike the majority of the other rickettsial diseases of man the blood-sera of patients suffering from trench fever do not contain antibodies that react with the O-antigens of Proteus X strains. Some regard the condition of the tongue as very characteristic, while the " spiking " of the secondary fever is highly suggestive, as are also the " shin pains." As a matter of fact, the clinical picture has to be studied as a whole and other diseases excluded by careful laboratory tests.

Differential Diagnosis.—Influenza, malaria, enterica, dengue, phlebotomus fever, relapsing fever, undulant fever and the milder forms of leptospirosis icterohæmorrhagica may be mentioned as the diseases most likely to be mistaken for trench fever.

Prophylaxis.—This consists chiefly in measures directed against lice. (*See* Section on Arthropod Pests.) The urine and sputum must be disinfected, as they contain the virus.

Treatment.—For the most part this is symptomatic. Aspirin, 20 grains at night, seems to be the best analgesic. Phenacetin and opium are useful. Mustard leaves ease the pains in the shins, as do hot belladonna stupes. When these and other pains are very severe lumbar puncture gives relief, but vinum colchici should first be tried, as it has been found helpful. Some employ Collargol, 10 c.cm. of a 1 per cent. solution intravenously, the injections being repeated at two or three-day intervals. Collargol has been proclaimed a specific cure in acute cases, but substantiation is lacking.

Rest, blood tonics, regulated exercise, and thyroid therapy are indicated for the subsequent debilitated condition.

SCHISTOSOMIASIS

Schistosomiasis in various degrees of severity is widespread in Africa, where both * *Schistosoma hæmatobium* and *S. mansoni* are represented. The native population of Egypt is heavily infected, and in some places as many as 90 per cent. of the inhabitants are victims of this distressing and crippling complaint. Although the disease varies in intensity in different parts of Egypt, a good practical rule is to regard the Nile itself and all districts subject to irrigation as potentially dangerous.

Endemic areas of infection with *S. hæmatobium* are known to exist in Mesopotamia, and a few cases of apparent indigenous origin have been reported from India, but further investigation is required on this point. In South America and the West Indies schistosomiasis appears to be due to *S. mansoni* only. *S. japonicum* causes the variety of the disease found in the Far East, the symptomatology of which will not be considered in this section.

Etiology.—The schistosomes constitute a family of sexually differentiated trematodes. Of the nine known species, two, *Schistosoma hæmatobium* and *S. mansoni*, seemingly occur as a natural infection in man only. *S. japonicum*, which causes the Far Eastern form of human schistosomiasis, is not peculiar to man but attacks domestic animals—cattle, horse, goat, dog, cat—as well. The six remaining species occur as natural infections in various animals, and it is possible that some of these schistosomes may on occasion attack man, a point to be considered when investigating the origin of sporadic cases of human schistosomiasis in localities where the disease is not known to be endemic in man. The habitat of these worms is the vascular system, and, in the adult form, *S. hæmatobium* is found in the portal vein and its branches and in the vesical, uterine and hæmorrhoidal veins, while *S. mansoni* inhabits chiefly the portal and mesenteric veins.

The male and female of *S. hæmatobium* live apart until mature. Then the female enters the gynæcophoric canal of the male. The latter is a small white worm about half an inch in length, the female is considerably longer and is more filiform (Fig. 71). *S. mansoni*,

* *Schistosoma* Weinland, 1858 = *Bilharzia* Cobbold, 1859.

though closely resembling *S. hæmatobium*, has certain structural differences. *S. hæmatobium* produces terminally-spined eggs, which are found usually in the urine, but sometimes in the fæces (Fig. 73). While the lateral-spined ova of *S. mansoni* are found usually in the fæces only, though rarely they may appear in the urine (Fig. 72).

A new schistosome, *S. intercalatum*, has recently been described, which deposits eggs with terminal spines in the human intestine, but not in the bladder.

The injury and irritation produced by these spined eggs are the initial cause of the symptoms. Work by Leiper and his colleagues has demonstrated the full life-history of the parasites and pointed the way towards prevention of the disease.

Fig. 71.

Schistosoma mansoni, male, and female within gynæcophoric canal. (After Looss.)

Fig. 72.

Lateral-spined egg of *S. mansoni*.

The egg, whether from the urinary passage or the rectum, if it reaches water, hatches into a ciliated free-swimming larva or miracidium which, unless it finds a suitable host, perishes in about twenty-four hours (Plate 28). The intermediate host—which, if found, it enters—is some species of fresh-water snail. In Egypt the whelk-like snail,* *Bulinus truncatus* (Plate 29 B), or the very similar

* According to Annandale, these three *Bulinus* are specifically identical, and should all be included in the one species, *B. truncatus*. *Bulinus truncatus* (Audouin, 1809) = *B. contortus* (Michaud, 1831).

B. dybowski and *B. innesi*, harbours the miracidium of the urinary *Schistosoma*, while the ammonite-shaped *Planorbis boissyi* (Plate 29 A) affords shelter to that of the intestinal worm. A species of *Planorbis* (*P. dufourii*) was shown to be an efficient intermediary for *S. hæmatobium* in Portugal.

In the snail the larva becomes a sporocyst which gives off many daughter sporocysts, and these, in their turn, produce vast numbers of bifid-tailed cercariæ (Fig. 74) which escape into the surrounding water. A single snail has been known to discharge 170,000 of these at the rate of over 2,500 a day. These tiny creatures can just be seen with the unaided human eye when in clear water in a test tube. A lens is required for their detection in natural water. To the naked eye they look something like a swarming mass of tiny white

Fig. 73.

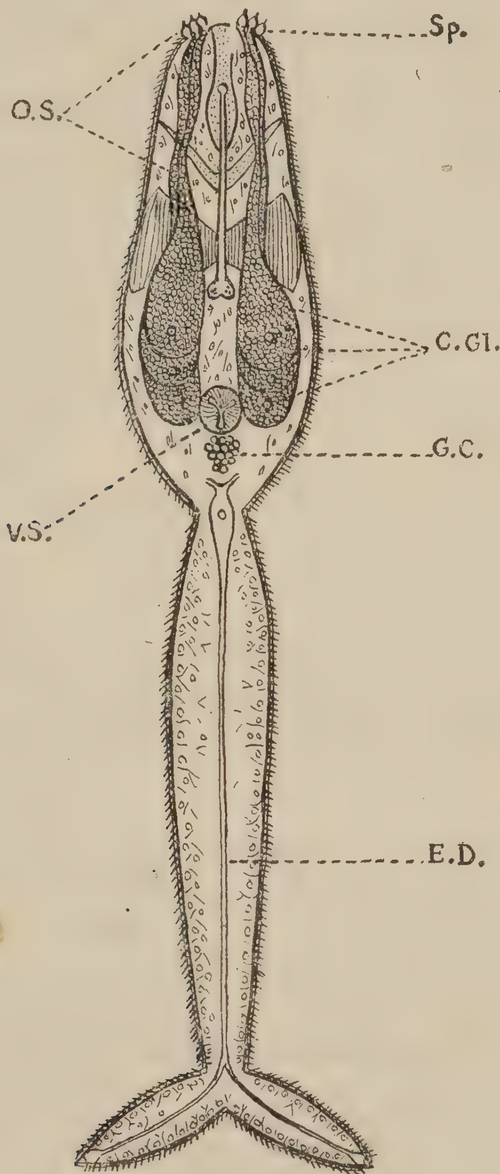
Terminal spined egg of *Schistosoma hæmatobium*.
(After Looss.)

hairs. Their expectancy of life in the free-living state is about thirty-six to forty-eight hours, and if they fail to get access to a human host within this time, they perish. They can penetrate the unbroken skin, and also pass through the intact mucous membrane of the mouth when being swallowed in water. The blood stream carries the cercariæ to the lungs, whence they may pass directly into the liver by way of the diaphragm, or they may pass through the lungs, return to the heart, and reach the liver by means of the blood stream. In the liver they develop into adult male and female worms, the process taking about two months to accomplish. Thereafter the females start producing the spined eggs.

Symptoms.—These may be very slight or exceedingly severe. In primary infections with *S. hæmatobium* the disease is usually mild, albeit intractable, and shows itself, generally some three months after infection, by the passage of bloody urine, with frequency of micturition and signs of cystic or urethral irritation. The rectal form may, at first, present no symptoms, but later, and especially in re-infections, the polypoid and ulcerated condition which is set up in the rectum leads to diarrhœa and dysentery of a special kind. Work on an outbreak amongst Australian troops in

Egypt showed that the incubation period of *S. mansoni* infection may vary from four weeks to three months. The most common period appears to be from four to eight weeks, a shorter time than is the case in the vesical disease. Some of the cases felt an itching

Fig. 74.



Cercaria of *Schistosoma mansoni.*

O.S.—oral sucker; V.S.—ventral sucker; Sp.—Spires; C.Gl.—Cephalic glands; G.C.—Germinal cells; E.D.—excretory duct.

of the skin on leaving the water where, as events proved, they had been infected while bathing. The early toxic symptoms as a rule began gradually with loss of appetite, persistent headache, pains in the back and limbs and dizziness. Cough was frequent and was

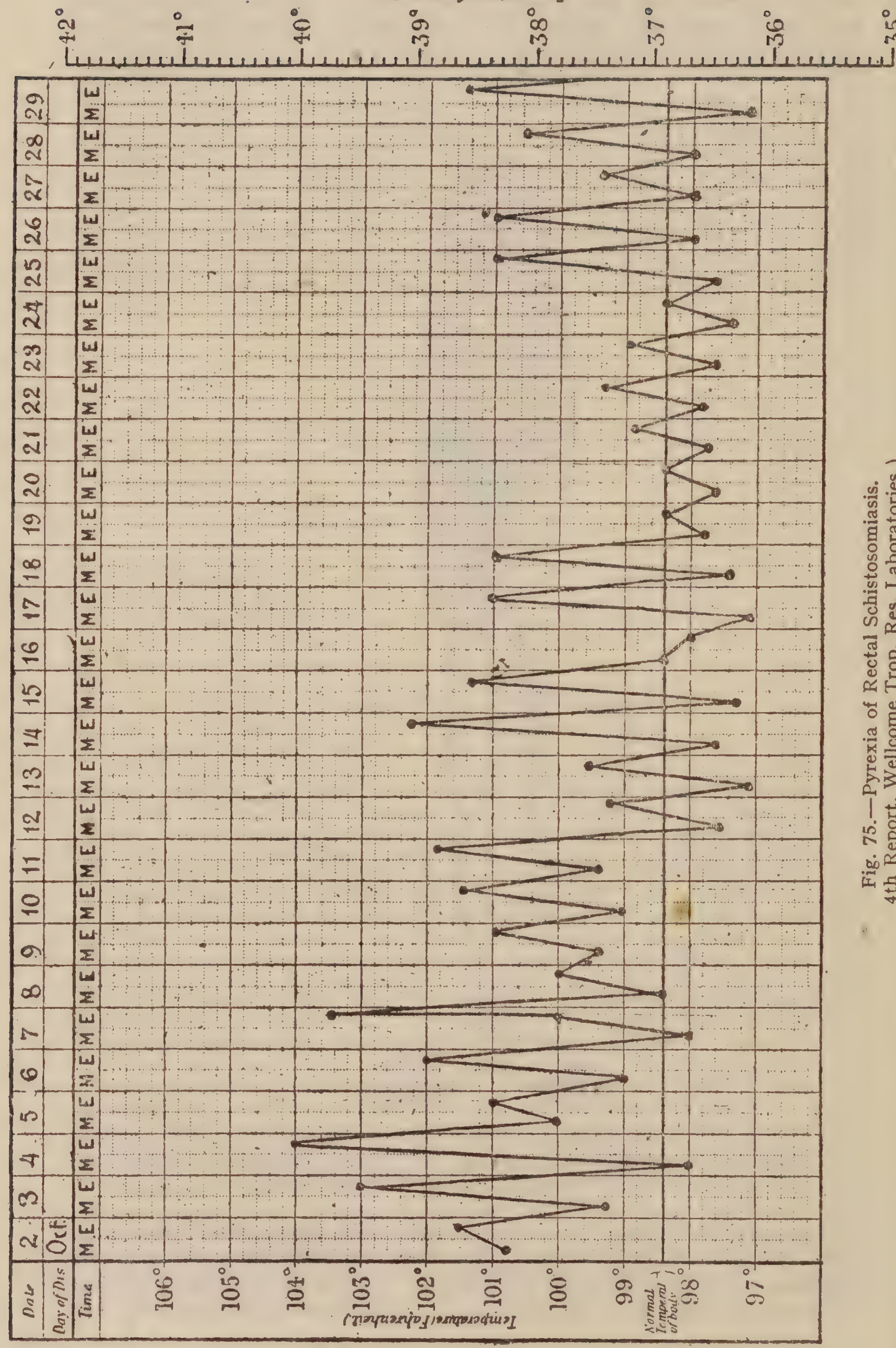


Fig. 75.—Pyrexia of Rectal Schistosomiasis.
4th Report, Wellcome Trop. Res. Laboratories.)

sometimes the first symptom. Later, abdominal pain, enlarged and tender liver and spleen, pyrexia associated with rigors and sweats, bronchitis, urticaria and diarrhœa were the chief features. The blood showed marked eosinophilia, but it should be noted that eosinophilia may be absent in schistosomiasis. A distended abdomen with tenderness over the descending colon may be present.

Later the toxic symptoms, which are evidence of a heavy infection, abate, and are usually followed by recurring attacks of diarrhœa and dysentery due to the ulcerative and polypoid lesions in the intestinal wall. The stools may be normal, and it may be very difficult to detect the ova. Remember that eggs may be easily found in scrapings made from lesions in the rectum when these are present. Cases have been known of prolonged schistosomal pyrexia in which the eggs were only found post mortem on scraping the bases of the intestinal ulcers (Fig. 75). In bad cases the lungs and liver suffer, the latter becoming cirrhotic, but as a rule there are no symptoms of such invasion. At the same time the urinary and intestinal trouble lead to invaliding from anæmia, marasmus, and the intercurrent diseases and sequelæ to which the victim of schistosomiasis is liable. In Africa *S. mansoni* appears to be a common cause of splenomegaly and of a form of hepatic cirrhosis known as "pipe-stem" cirrhosis.

Diagnosis.*—This depends on the microscopical examination of the urine or fæces and the finding of the characteristic eggs.

The complement fixation and dermal tests devised by Fairley may be helpful in establishing a diagnosis in doubtful cases.

Differential Diagnosis.—Care should be taken not to confound a chronic amœbic or bacillary dysentery with one due to schistosome infection. The above-mentioned outbreak showed that rectal schistosomiasis had also to be distinguished from enterica, urticaria, pulmonary tuberculosis and hepatic abscess. Appendicitis is another condition which it may resemble.

Treatment.—The specific treatment for schistosomiasis is the intravenous administration of antimony tartrate, which in this disease is superior to the pentavalent compounds. The methods of preparing and injecting the solutions are described on page 135 and need not be repeated here. It is usual to commence treatment of schistosomiasis with an initial dose of about ½ a grain of the salt selected. The injections are given every other day, with a maximum dose of 2 or 2½ grains. As the dose increases, some prefer to give the injections at two-day intervals. A course consists usually of about 20 to 30 grains in all, but, as in all other diseases which are cured by the injection of antimony, there is no universal curative dose, and each case must be judged on its own merits.

Emetine has definite curative properties in this disease, and is the treatment of choice for children where intravenous injections are difficult. For a child of nine years Cawston recommends a total dosage of 9 grains, given intramuscularly, spread over twenty-

* Sigmoidoscopy and cystoscopy, in their respective spheres, are often of great assistance in the diagnosis of schistosomiasis.

four days, the maximum dose being $\frac{1}{2}$ grain. Within the same period children of twelve years usually require 12 grains, and those of fifteen 15 grains to effect a permanent cure. Two-thirds of a grain, and 1 grain respectively, are the usual maximum doses. To counteract cardiac depression some such drug as sparteine ($\frac{1}{10}$ to $\frac{1}{5}$ grain) may be injected along with the emetine.

As treatment takes effect, the ova passed out may be seen to be dark, shrivelled or distorted in appearance, and they do not hatch out when placed in water.

Anthiomaline, a lithium salt of antimony, is well reported on. Injection into the deltoid muscle of 3·0 to 3·25 c.cm. of anthiomaline, three or even four times a week, would seem to have effected cure of *S. hæmatobium* infestation in three weeks among out-patients continuing their work, though reporting some generalized muscular pain. This would indicate that the eggs are disintegrated and the worms destroyed most readily by giving the drug sufficiently often to prevent their recovering from one dose before the next and before much of the drug already given has been eliminated.

With *S. mansoni* infestations escape of the eggs is too uncertain to be much of a guide as to when treatment may safely be discontinued and 25–30 grains of tartar emetic is needed until such time as careful investigation has revealed the clinical equivalent of anthiomaline.

Prophylaxis.—This is most important and consists in the strict avoidance of any kind of personal contact with water which may by any possibility be infected. The Nile and its canals, the lesser irrigation channels, the waters of swamps and marshes, and any permanent collections where the snail hosts may occur are to be viewed with suspicion.

Unfiltered water from such sources is dangerous unless it has been stored for at least forty-eight hours after being drawn.

Bathing, wading, washing and drinking in such waters must be forbidden.

Clothes, unless waterproof, are no protection to the wader. Gloves and more especially rubber gloves should be worn by those examining possibly polluted water for snail hosts or mosquito larvæ, while men such as engineers working in such water should be protected by rubber thigh boots and gloves.

To ensure a safe water supply the following measures should be adopted :—

(*a*) Weed on which the snails feed should be removed, and, if possible, infected water channels should be drained dry and sun-baked, the snails being killed by this means.

(*b*) Chemicals, such as copper sulphate in amount equivalent to 1 lb. per 100,000 gallons (1 part per million), should be used for the destruction of snails.

(*c*) Snails may be eliminated from water supplies by means of a screen 16 meshes to the linear inch placed between the source and the intake.

(*d*) Cercariæ, while not being eliminated by ordinary methods of filtration such as shallow sand filters, etc., may possibly be

excluded by the Stellar and Meta filters, which are now fitted to army water trucks and trailers.

It should be noted that the apparent efficiency of filtration on a large scale, as for a town or city, is to be partly explained by the length of time intervening between the collection of the water and its consumption, which usually exceeds the minimum of forty-eight hours' storage required to ensure the death of cercariæ. It should be noted that sedimentation of water, with or without the use of chemicals, is not effective alone in dealing with cercariæ.

(*e*) Certain chemical methods of destroying cercariæ are valuable. Superchlorination, as employed in the army, kills the cercariæ in 30 minutes ; chloramination in doses of 3 parts per million is effective in 60 minutes ; whilst sodium bisulphate, 1 in 1,000, is immediately lethal.

As regards the treatment of water not required for drinking purposes, cresol, 1 in 10,000, will render it safe immediately ; if stored overnight 1 in 90,000 is sufficient.

SCURVY

Scurvy results from severe and prolonged deficiency of vitamin C, and is characterized by weakness, loss of weight, anæmia, swelling and ulceration of the gums, and multiple hæmorrhages. In its classical form it has been known for centuries and has been recognized as a disease of sailors, soldiers, prisoners, and the poor—in fact all whose diet was meagre and lacking in fresh food and who were subjected to exposure and physical strain.

Frank scurvy is comparatively rare to-day, except during war and famine ; but hypovitaminosis C, otherwise known as subclinical or latent scurvy, is common. Subclinical scurvy is an ill-defined condition presenting few or none of the features characteristic of scurvy, and it can be recognized only by the presence of vague non-specific symptoms and signs, the evidence of an inadequate intake of vitamin C, and certain laboratory tests.

Etiology and Pathology.—Vitamin C, lack of which ultimately leads to scurvy, has been identified as ascorbic acid, a six-carbon-chain acid related to the hexuronic acids which are themselves derived from the simple hexose sugars. It is a powerful oxidation-reduction agent capable of reducing many organic compounds, in which process it is reversibly oxidized to dehydro-ascorbic acid which is also biologically active ; this substance is readily reduced back to ascorbic acid, but is also very susceptible to further oxidation into biologically inactive compounds.

Vitamin C cannot be synthesized in the human body, and man has therefore to obtain it from his diet. It is found in the circulating blood in amounts which seem to depend on the general level of the vitamin in the tissues ; it also occurs in the cerebro-spinal fluid and in secretions such as tears, perspiration, and milk.

Ascorbic acid is lost from the body through its utilization in metabolism and through its excretion in the urine. The urinary excretion reflects in a general way the state of vitamin C nutrition of the body, but even when the intake is low, a certain amount of vitamin C is excreted.

Vitamin C, although stable to air and daylight in pure, dry crystalline form, is very easily oxidized in aqueous solution unless this has an acid reaction and is free from catalysing agents such as traces of copper. The vitamin C of foodstuffs is also easily destroyed under such conditions as drying, ageing, storing and prolonged cooking, especially if the solution is alkaline.

While the biological activity of vitamin C as an oxidation-reduction agent has been recognized for some time, little is known as to how this activity accomplishes the function of vitamin C in the body. This function appears to be the maintenance of the normal structure and formation of mesodermal tissue and structures derived from such tissue, such as bone, teeth, capillaries, and connective tissue. Vitamin C seems to be necessary for the formation of the collagen bundles in the intercellular ground substance; in vitamin C deficiency this intercellular ground substance becomes defective and the collagen bundles disappear. This effect of deficiency is easily recognizable histologically in connective tissue, and it also accounts for the changes in particular structures such as capillaries, bone, teeth and gums.

The site of the lesion of the capillaries is uncertain, but the result is that the capillary wall becomes defective with resultant hæmorrhage in many parts of the body. The hæmorrhages in the skin are characteristically perifollicular petechiæ, but there may also be large areas of ecchymosis. Deep hæmorrhages may also occur subcutaneously or intramuscularly, especially in the lower limbs. Subperiosteal hæmorrhages are rare in adults, but common in children. Epistaxis is often seen and there may be hæmorrhages into serous cavities, and more rarely, from the gastro-intestinal tract. Capillary weakness also leads to œdema, especially in the legs.

The skeletal changes are a prominent feature of scurvy in infants and children, in whom the proximal end of the tibia and humerus, the distal end of the femur and the costochondral junctions are the sites most often affected. The osteoblasts lose their shape, come to resemble fibroblasts, and instead of bone produce collagen and fibrils. This change occurs chiefly at the metaphysis, where a zone of rarefaction consisting of fibrous tissue results, which may be the cause of separation of the epiphysis. There is also thinning of the cortex throughout the whole length of the long bones. The periosteum is loose and easily raised, and subperiosteal hæmorrhages are common. The changes in the teeth consist in degeneration of the odontoblast layer, with degeneration of the dentine and its replacement by osteoid tissue. Rarefaction of the alveolar processes may cause loosening and loss of the teeth.

The gums are only affected when there are teeth, so that infants and edentulous persons may fail to show one of the most characteristic lesions of scurvy. Scorbutic gingivitis begins with redness of the interdental papillæ due to hyperæmia, followed by swelling, hæmorrhage, retraction, ulceration and secondary infection. In

advanced cases of scurvy, atrophy of the bone-marrow leads to anæmia.

Symptoms.—Scurvy begins insidiously, early symptoms being loss in weight, progressive weakness, pallor, sometimes formication in the soles of the feet and stiffness in the leg muscles. Later the gums become affected, the first sign being a soft swelling sprouting up *between* the teeth. At the apices of these swellings red "buds" (Plate 30) appear, and these become "blossoms" resembling in shape an opening rose. The blossoms spread and unite, the gums become swollen and spongy, and ulceration and bleeding occur. Very often the typical gums are at first seen only round the molar teeth or carious stumps. Both the palatal and buccal sides of the alveolus may be affected. As the disease progresses the teeth become loose, and in extreme cases the gums present large fungating masses pushing out the cheek. Sheppard states that very early scurvy gums often show a "rolled" edge with fine, parallel, claw-like striations running across it. This is never seen in pyorrhœa. The tongue becomes swollen, the breath very foul, the salivary glands may enlarge. Hæmorrhages under the buccal mucous membrane are common. Other hæmorrhages occur. A very early sign is the presence of petechial hæmorrhages *round the hair follicles* of the thigh. Later they may be seen on the arms and trunk. Their relation to the hair follicles is important in diagnosis. Muscular hæmorrhages affect the muscles which have most work to do. In soldiers they are as a rule most common in the leg muscles. They cause a bulging of the muscle, often evident to the eye, but best detected by measurement. Hæmorrhages round or near a joint may interfere with its movements. Other sites are under the periosteum, especially that of the tibia, and at the junction of the costal bones and cartilages, forming the scurvy rosary, usually a late symptom.

Any injury is apt to be followed by a hæmorrhage. Another important symptom is œdema, often first visible round the tendo achillis and then spreading round the ankles to the dorsum of the foot. It is best seen by viewing the feet from behind. The hæmorrhages and œdema cause pain and stiffness, as does the brawny induration which affects muscles and subcutaneous tissues. It often fills up the popliteal space. Bleedings from various mucous membranes may occur. Those from the bowels when copious are very serious. Other symptoms are anæmia with its associated heart conditions, impaired appetite, and mental depression. As a rule it is only in advanced cases that there is any rise of temperature, but pyrexia has been reported as a concomitant of one epidemic. Death occurs from gradual heart failure, sudden syncope or an intercurrent infection.

These symptoms and signs of classical scurvy make up a characteristic clinical picture, but the much more common condition of latent or subclinical scurvy is very difficult to recognize; for the symptoms are few, and largely non-specific. The most frequent early sign of vitamin deficiency is probably gingivitis, although it must be emphasized here that all gingivitis is not due to lack of vitamin C. Apart from the gingivitis, hypovitaminosis C may be marked by

weakness and malaise, slight pallor and anæmia, loss of weight, and vague pains in the limbs, and such symptoms occurring in conditions where the intake of vitamin C appears insufficient should suggest early vitamin C deficiency.

The vitamin C requirements of the body are increased by conditions producing increased metabolism; for example, severe exertion and fevers. For this reason, symptoms of vitamin C deficiency may complicate any febrile illness, even in the presence of an otherwise normal vitamin C intake.

Diagnosis.—Vitamin C deficiency is diagnosed on the evidence of deficient vitamin C intake, the clinical picture, capillary resistance tests and certain laboratory tests.

These last depend on the ease with which vitamin C can be determined in the blood and urine by the decolorization of the blue dye dichlorphenolindophenol by vitamin C, and include the following investigations :—

1. Determination of the *vitamin C excretion* in the 24-hour urine. Although the daily vitamin C excretion varies widely, there is a lower range of excretion below which persons on a reasonably good vitamin C intake seldom fall. Values below 15 mg. of vitamin C in the 24-hour urine suggest a deficiency, but give no indication of the severity of the deficiency ; this requires the use of the saturation test.

2. Determination of the *concentration of vitamin C in the blood.* The level of blood vitamin C is easily influenced by temporary variations in the vitamin C intake, so that this test must be done while the individual is in the fasting state and should be repeated on successive days. No definite standards have yet been established, but is generally accepted that in normal vitamin C nutrition, the plasma ascorbic acid concentration should be at least 0·7 mg. per 100 c.cm., while values persistently below 0·2 mg. per 100 c.cm. indicate severe vitamin C deficiency.

3. The *saturation test.* This consists in administering a standard dose of vitamin C and observing its effect on the blood or urine vitamin C content. The usual procedure is to administer a standard dose of 600 mg. of ascorbic acid until a definite plateau of vitamin C excretion in the urine is reached, indicating that the body tissues are now saturated with vitamin C. On the assumption that saturation with vitamin C represents the physiological optimum, then the extent of the vitamin deficiency in any individual is given by the number of doses required to produce saturation. For practical purposes, the excretion of 50 mg. of vitamin C in the urine passed between the end of the third hour and the end of the sixth hour after the administration of the test dose is taken to indicate saturation.

While classical scurvy is readily diagnosed, the latent or subclinical form will require one or more of these laboratory tests for its recognition.

Differential Diagnosis.—Distinguish from beriberi, purpura, rheumatism and a malarial syndome simulating scurvy. It is very important and often difficult, especially in the case of Indian troops and followers, to distinguish scorbutic gums from pyorrhœa. All that bleeds on slight pressure is not scorbutic. Sheppard gives the following useful notes on pyorrhœa alveolaris :—

"The early stages show slight swelling followed by an eating away of the gum margin. These changes occur *over* the teeth and not between them as in scurvy. The later stages are characterized by marked shrinking of the gums over the teeth, whereby the roots are exposed encrusted with tartar. In either stage pus may be squeezed from between the gums and the teeth. This condition is almost confined to the lower incisors and canines. Occasionally cases of pyorrhœa show hypertrophy of the margins of the gums. In these cases the gums are fairly hard, and between them and the teeth lies a trough of pus. Scurvy and pyorrhœa are distinct diseases. They may possibly occur simultaneously, but the one does not necessarily predispose to the other."

Prophylaxis.—The presence of sufficient anti-scorbutic elements in the dietary must be ensured. The vitamin (vitamin C) is present to a lesser or greater extent in all fresh raw foodstuffs. The richest sources are fresh fruits and their juices and green vegetables, and of particular value are oranges, lemons, grapefruit, and tomatoes. Lime juice as ordinarily prepared is useless in the prevention of scurvy, whilst fresh limes are of considerably less value than lemons. Potatoes, swedes, onions, and other roots and tubers are fair sources, while meat and milk contain the vitamin in small quantities only.

Vitamin C is deficient in canned and dried foods, but improved methods of canning have resulted in less destruction of the vitamin, and tinned tomatoes particularly are a valuable source. In selecting vegetables for a campaign in the tropics it is important, as far as circumstances permit, to select those which stand transport well. Onions and potatoes are both valuable in this respect ; the latter may be eaten raw, preferably made up into a salad with chopped up onions and vinegar.

Under exceptional circumstances when the provision of sufficient vitamin C in the ordinary elements of the diet is impracticable, the issue of tablets of ascorbic acid may help to solve the problem. One tablet containing 25 milligrammes of ascorbic acid made up with sugar to give bulk should, under these exceptional circumstances, be taken daily by each man. Vitamin C is very rapidly oxidized by heat or alkalies so that prolonged cooking or the use of soda in the cooking-pot should be prohibited. Frying is less destructive. The vitamin is oxidized by prolonged heating such as takes place when stewing. Vegetables should be cooked for as short a time as possible. Green vegetables should be obtained fresh, and should be stored, if storage is necessary, in a cool, damp place. In cooking, green vegetables should be placed in boiling water, a small amount at a time, so that the water does not go off the boil with each addition ; they should be cooked only long enough to make them tender (20–30 minutes) and served at once. Keeping green vegetables or potatoes hot after cooking causes rapid destruction of vitamin C.

A considerable amount of vitamin C (as well as vitamin B_1 and minerals) is extracted into the cooking water when green vegetables are boiled, and this vegetable water should therefore not be discarded, but used as a stock for soups and gravies. Peeling, chopping or crushing of vegetables and fruits tends to break down the cell walls and leads to more rapid oxidation of the vitamin.

While a relatively small intake of vitamin C will prevent scurvy, it is now widely accepted that mere protection against scurvy does not constitute optimum vitamin C nutrition, and that an adequate intake is the amount which will keep the body tissues more or less saturated with the vitamin. On this basis, while an intake of 25 mg. of vitamin C, or even 15 mg., will protect against scurvy, the optimum intake is now considered to be about 50–75 mg. daily.

The vitamin C content of foodstuffs can be obtained from food tables, but at least half must be deducted to allow for loss of vitamin in the preparation and cooking of food.

Tinned and preserved meats possess no antiscorbutic value. Frozen meat is more valuable and should be roasted when possible. Fresh meat contains more vitamin C than frozen meat, but some 2–4 lb. a day are required to prevent scurvy, and, on the whole, meat has little antiscorbutic value.

Pulses, beans, peas, and lentils in the dried condition have no antiscorbutic value, but this develops if they are allowed to germinate. Pulses are also rich in vitamin B.

The method adopted for germination is as follows. The beans, peas, or lentils are soaked in water at room temperature (60° F.) for twenty-four hours. The water is then drained away and, to permit germination, the soaked seeds are spread out in layers, not exceeding 2 to 3 inches in depth, and kept moist for a period of about forty-eight hours at ordinary room temperature. They should not be allowed to dry after this operation, but should be cooked as rapidly as possible (lentils 20 minutes; peas 40 to 60 minutes).

In addition to the dietetic measures outlined above, certain other points require attention in connection with the prevention of scurvy. Oral hygiene must be looked to and the toothbrush used regularly; dental floss should also be used. Overcrowding and insanitary and debilitating conditions must be avoided, and everything possible done to maintain at a high level the general health of the men.

Treatment.—The symptoms of scurvy and hypovitaminosis C respond quickly to the administration of adequate amounts of vitamin C, clinical improvement often appearing within a matter of hours.

It is immaterial whether the vitamin is given in natural foodstuffs rich in it, or as synthetic ascorbic acid, since the latter can completely cure scurvy. In both mild and severe cases, a diet containing a liberal supply of vitamin C (about 100 mg.) should be given. In mild cases it will be sufficient to add another 100 mg. of vitamin C to the diet, either as foods rich in vitamin C, such as citrus fruit juices, or as synthetic ascorbic acid. In severe cases, and in those where the patient cannot or will not take an adequate amount of vitamin-containing food, synthetic ascorbic acid should be given in large amounts—up to 500 mg. daily. While oral administration is usually satisfactory, the vitamin may also be given intravenously.

Large doses should be continued until a good clinical response has been obtained and the urinary excretion of vitamin C shows that saturation of the body tissues has been achieved. The dose should then be reduced to a maintenance one of about 100 mg. until the patient can be placed on a diet with an adequate vitamin C content.

Local treatment is usually unnecessary, since all the lesions respond rapidly to vitamin C; but a mild astringent mouth-wash may be used where mouth lesions are severe.

SICKLE-CELLED ANÆMIA

Sicklæmia consists in a tendency, inherited as a Mendelian dominant, for the red blood corpuscles, under certain conditions, to assume bizarre forms with sharply-pointed and filamentous projections. The most usual shapes resemble crescents or oat cells, but curious granular forms may also be seen.

Sickling is a reversible phenomenon directly related to oxygen concentration. The red cells are sickled when the hæmoglobin is in the reduced form, and they return to their normal discoid shape when it is combined as oxyhæmoglobin.

The condition is seen three times more often in men than in women. It is probably the commonest cause of anæmia in adult Africans, and is said to affect 5–10 per cent. of negroes and mulattoes; but it has also been recognized in Greeks, Syrians, Italians and others of Mediterranean races in whom negroid ancestry can be excluded. Before diagnosing it in a person of European stock it is necessary to exclude ovalocytosis, in which the red cells are oval, like those of a camel. This, too, is inherited as a Mendelian dominant but it causes no disability.

Sickling may manifest itself in two forms: (*a*) an acute hæmolytic anæmia, with exacerbations arising at intervals for no apparent reason, or (*b*) with acute infections. In America it is said to be associated with ulceration of the legs.

Pathology.—When the red cells assume bizarre forms the blood begins to stagnate in the vessels, causing anoxæmia and thus increased sickling. Thrombosis is found in end-arteries, and infarcts followed by necrosis appear in many organs. In children or adults dying after one or two hæmolytic crises the spleen is enlarged, showing areas of congestion and actual hæmorrhage round the central arterioles. Later the hæmorrhagic areas are replaced by fibrosed nodules containing brown pigment, and after repeated attacks of acute anæmia the spleen becomes small and atrophied, sometimes weighing only 2–3 oz. The other organs are pale after death from acute hæmolysis, with small infarcts in the kidneys and lungs. In the liver the intracellular canaliculi are distended with bile. The right side of the heart may be dilated. Osteoporosis of the long bones and thickening of the skull are not uncommon. The bone-marrow may also show hyperplasia, associated with the presence of fat emboli in various organs.

Symptoms.—During the acute hæmolytic crisis there is increasing pallor, jaundice, bilious vomiting, dyspnœa, headache and dizziness. The urine may contain hæmoglobin and albumin and the clinical picture may closely resemble blackwater fever, especially when anuria develops. The hæmoglobin may be reduced to 30 per cent., the total red cell count falling from 1 to 3 million per c.mm. ; normoblasts are common, polychromasia is marked and reticulocytes may form 25 per cent. of the circulating reds. Phagocytosis of the red cells by circulating monocytes may be seen and a neutrophil polymorphonuclear leucocytosis of from 10,000 to 30,000 per c.mm. is usual. Coagulation time and platelet count are normal. A positive indirect van den Bergh reaction is obtained, with a raised icteric index.

Anæmia, however, may not be the primary symptom. There may, for instance, be severe abdominal pain which may simulate the gastric crisis of tabes, while patients suffering from sicklæmia have been mistakenly operated on for appendicitis, cholecystitis or even perforated gastric or duodenal ulcer. In other cases the heart sounds and cardiac enlargement may suggest mitral stenosis or other valvular lesions . Severe pain may be felt in the muscles, long bones and joints, mimicking acute rheumatism except that the pain is not relieved by salicylates. In some instances a single joint may become swollen and tender, with effusion into the cavity, and gonococcal infection may be wrongly diagnosed.

Sicklæmia may also cause nervous symptoms, drowsiness or coma, hemiplegia, aphasia, headache, convulsions, stiffness or pain in the back and neck, irritability, weakness of the facial muscles, ocular disturbances and cerebral vomiting. As the lesions are usually intracranial, and hæmorrhage is very rare, examination of the cerebrospinal fluid gives no reliable information though the fluid may be under increased pressure. The relationship between sicklæmia and ulceration requires further study, as does the possible connection between sicklæmia and the not infrequent occurrence of jaundice in Africans suffering from lobar pneumonia.

Diagnosis.—A drop of blood from the finger is placed on a clean slide and covered with a cover-slip. The slip is immediately ringed round with vaseline or Canada balsam to exclude air. The sealed preparation is then kept either at room, or preferably at body, temperature and is examined microscopically at intervals up to 24 hours. The rapidity with which sickling develops, and the percentage of red cells sickled in a given time, provides an indication of the severity of the condition. Normal blood will not sickle. The test can also be carried out with oxalated blood.

Sickling in the blood-stream can be detected as follows : 0·25 c.cm. of liquid paraffin is taken into a 2 c.cm. sterile syringe ; all air is expelled ; 0·25 c.cm. of blood is then removed from a vein and immediately expelled into a test-tube containing 1 c.cm. of 10 per cent. formalin in saline, protected from the air by a layer of liquid paraffin. The needle of the syringe is passed through the liquid paraffin into the formalin and the blood expelled. After allowing fifteen minutes for the red cells to be fixed they can be removed and examined microscopically. Sickling *in vivo* is usually associated with a hæmolytic crisis.

Tissues removed post mortem, fixed in formol and sectioned will show sickle cells within the blood-vessels.

Treatment is purely symptomatic. With an acute hæmolytic crisis and a rapid fall in hæmoglobin repeated blood transfusion may be necessary. Where there is sickling but not anæmia administration of liver extract or yeast extract may decrease the chances of an acute hæmolytic crisis by rendering the bone-marrow less hyperplastic.

SKIN DISEASES

All manner of skin complaints occur in the sub-tropical and tropical areas. Even when trivial they are apt to be disabling. Some, such as oriental sore and scabies, are of such importance that they are dealt with separately (pages 178 and 22). Here only a few are considered, ranging from the painful if comparatively harmless boil to the destructive *Ulcus tropicum*, a very serious complaint. Skin diseases are commonest and worst in damp and humid localities like the East African littoral and the shores of the Persian Gulf, but drier regions have their own special infections, as witness the veldt sore of Egypt and Palestine, and the oriental sore of Mesopotamia.

FURUNCULOSIS

Boils are troublesome in many tropical areas. Men are apt to suffer from them when they are " run down," and campaigning conditions in hot climates tend to produce debility. During the last war they were very common in East Africa during or after the rain and in Egypt and Palestine during the hot damp summer, especially near the sea-coast. The so-called Nile boil is only too well known.

Etiology.—The bacteriology of tropical boils has been the subject of a good deal of research. The most common organism associated with them is *Staphylococcus aureus*, but it appears that in Egypt, at least, a white staphylococcus is to blame in many cases, especially those of a severe type.

Symptoms.—These do not require a lengthy description as everyone is familiar with the appearance of a boil. In the tropics they are often multiple and a very favourite site is the buttocks. Any part, however, which is apt to be bathed in sweat is liable to infection. A boil on the face may apparently result from the bite of a mosquito or other blood-sucking insect. The true Nile boil usually begins at the base of a hair follicle.

Sometimes in debilitated persons boils run a prolonged course, continuing to discharge and refusing to heal. As they are usually multiple, the unfortunate patient may be incapacitated for work.

Complications.—Lymphangitis and lymphadenitis may be mentioned.

Differential Diagnosis.—The occurrence of anthrax pustules following the use of infected shaving brushes must be kept in mind when a boil appears on the face, but the developed anthrax pustule is not like a typical boil and a bacteriological examination reveals the bacillus. When boils are numerous and persistent examine the urine to exclude diabetes.

Prophylaxis.—Protection from insect bites of all kinds should be ensured as far as is practicable. First-aid treatment should be made easily available for abrasions and other minor injuries sustained at games and other forms of recreation.

The provision and the enforcement of the use of adequate ablution facilities are important, while cleanliness of underclothing should receive constant attention with satisfactory laundering arrangements.

It must be remembered that dietetic defects are often a factor in the causation of furunculosis and a sufficiency of vitamins in the diet must be ensured. Excessive consumption of carbohydrates, especially in warm climates, should be discouraged.

If a boil develops it should be covered with a small dressing to prevent spread to other parts during washing, etc., or through the agency of flies.

Often the only effective preventive or therapeutic measure is a change of climate.

Treatment.—When a boil is very small it may be aborted by injecting into its centre one drop of pure carbolic acid, or by dipping a sharpened wooden match or a toothpick into the carbolic and thrusting it repeatedly into the heart of the furuncle. This method is somewhat painful but usually effective. If it is decided not to attempt to abort the boil it should be treated by heat, preferably by kaolin poultices. When suppuration occurs the boil may be opened by a small incision ; and when the boil has been incised, 10–12 per cent. sodium sulphate lotion may be used in order to promote drainage.

Vaccine therapy is of value in some cases of chronic furunculosis. Autogenous vaccines are preferable to stock preparations. Fifty million organisms is a usual initial injection. Of the sulphonamide drugs, sulphathiazole probably gives the best results, but details of dosage are still a matter for investigation.

It is important to raise the patient's resistance by giving him a carefully selected and well-balanced diet.

VELDT SORE OR BARCOO ROT

This is a chronic, septic ulcerated sore occurring in hot, dry, sandy or desert parts of the tropics and sub-tropics. It is found in the Middle East, South Africa, Iraq, the dry hot areas of India, and Northern Australia.

Etiology.—Vitamin deficiency may be a predisposing factor. Exposure of an abrasion to the hot sun may, by diminishing the skin's resistance, play a part in the production of these sores. A great variety of organisms have been isolated, including streptococci,

diphtheroids and staphylococci. A true diphtheria skin infection may occasionally occur in these sores.

Symptoms.—The lesions are usually found on the exposed parts of the body, especially the dorsal parts of the hands, forearm, elbows, knees and occasionally on the face. It may begin as an ordinary neglected traumatic abrasion or as a painful vesicle which breaks down. The sore in the chronic stage is usually seen as a depressed circular or oval indurated ulcer with a sloughing base often filled with crusts of greenish pus and surrounded by a hard bluish or inflamed edge. There is usually little complaint of pain. These sores may persist for months if not properly treated.

Differential Diagnosis.—Oriental sore is distinguished by the presence of *Leishmania tropica*. A careful bacteriological examination should always be made to exclude any specific pathogenic organism.

Treatment.—*Prophylactic*—adequate dietary and first-aid treatment of abrasions or sores as soon as they occur.

Curative—rest of the affected part, specific treatment of any pathogenic infection, otherwise treatment on ordinary surgical lines.

ULCUS TROPICUM

This form of phagedænic ulcer in contradistinction to veldt sore is met with in damp, steamy, tropical climates. The lower limbs are generally affected and a history of preceding trauma is common.

Etiology.—This is somewhat obscure. Some regard it as due to a dietetic deficiency; the debilitated are most susceptible. *Treponema schaudinnii* and fusiform bacilli are commonly present in the ulcers (Plate 31). Various cocci, fungi, diphtheroids, and true diphtheria bacilli may be found.

Symptoms.—The seats of election for tropical ulcer are the lower third of the leg, the ankle and the dorsum of the foot, *i.e.* parts liable to traumatism. It may occur elsewhere and is known to produce a form of ulcerative onychia.

There is usually only a single ulcer, but two or more may occur.

The lesion begins as a small, tender and often itchy papule or bleb with a dense inflammatory areola. An ulcer soon forms which is more or less painless and the edges of which tend to shelve and are not raised or thickened. It is usually covered by a most malodorous, greyish, purulent secretion. The surrounding skin is frequently œdematous. At first the sloughing process spreads rapidly and the centre of the ulcer may become funnel-shaped. In certain cases after ten days or so the slough is thrown off and a slow healing process sets in, the destruction being confined to the more superficial parts. Often, however, the disease attacks the deeper tissues and destroys everything in its course, eating its way through fascia, tendons, blood-vessels and bones and causing loss of life or loss of a limb or at the least producing great deformity and contractures.

Diagnosis.—In humid tropical climates a diagnosis is generally easy, though varicose ulcers, yaws, syphilitic and blastomycotic ulcers may need differentiation.

Treatment.—On the assumption that there is a deficiency factor present, and a nourishing diet, calcium, with added vitamins, should be given. Rest to the affected part should be secured. The ulcer should be cleansed by ordinary surgical measures. Sometimes healing can be hastened by scraping the affected part and dressing with :—

Brilliant Green	1·0 g.
Crystal Violet	1·0 g.
Alcohol (50 per cent.)	300 c.cm.

Recent reports on the treatment of these ulcers with sulphanilamide powder and strapping are encouraging. After cleansing the ulcerated surface and bathing it in hypertonic sod. sulph. solution, sulphanilamide powder is applied to the ulcer, which is then covered over with zinc oxide plaster and left for five days. Healing sometimes results in seven to ten days. In very resistant cases excision followed by skin grafting may be necessary.

TINEA CRURIS

Tinea cruris (dhobie itch) is one of the commonest skin complaints of the tropics and was very prevalent in 1914–18 in many war areas, perhaps more especially in Egypt and East Africa. It is worst during hot, damp weather, and may cause considerable suffering.

Etiology.—The eruption is usually caused by the fungus *Epidermophyton inguinale*, but occasionally other ringworm fungi may be isolated from the lesions.

Symptoms.—The crutch and the axillæ are the regions attacked. Intensely itchy, red, spreading patches develop which have characteristic raised well-defined margins; hence the old term " eczema marginatum " (Plate 32).

The irritation is worse at night, and often subsides during the cold weather, the areas affected becoming dry, scurfy and pigmented. The fungus is still present, though quiescent, and becomes active again under warm conditions.

Prophylaxis.—Wear clean cotton drawers, bathe frequently and use a dusting powder.

Treatment.—Mild cases readily yield to an ointment containing resorcin 1 drachm, salicylic acid gr. 10, and 4 drachms each of vaseline and lanoline.

Pigmentum carbol-fuchsin is a useful remedy; it should be applied twice daily. This paint may often be used successfully in cases in which there is considerable inflammation and which would be aggravated by an ointment.

Painting with iodine is often efficacious, but on no account apply this remedy to the scrotum. Continue to paint the affected parts daily until a considerable degree of reaction occurs, and then employ a dusting powder. When the irritation is allayed, the painting may be recommenced if necessary. Reinfection must be prevented by wearing cotton drawers disinfected daily by boiling or by careful ironing.

Deek's ointment often proves efficacious:

Ac. salicyl.	4 per cent.
Bism. subnit.	10 ,,
Hydrarg. salicyl.	4 ,,
Ol. eucalypt.	10 ,,
Lanoline and Vaseline to make up ...	100 ,,

(This ointment is very useful in some cases of *pruritus ani* and *vulvæ*, presumably of a parasitic nature. For this purpose dilute the ointment to half its strength to begin with.)

Bad cases require a 2 to 5 per cent. chrysarobin ointment employed with due warnings and precautions, and never prescribed when there is any renal infection. Dithranol, a substitute for chrysarobin, may be used as an ointment of 0·25 to 3 per cent. strength.

Interdigital Ringworm.—Epidermophyton not infrequently attacks the skin of the feet, particularly between the 4th and 5th toes. Pigmentum carbol-fuchsin is a satisfactory application for the majority of cases, the cure being completed with Deek's ointment or salicylic and benzoic acid ointment.

TRICHOMYCOSIS CAPILLITI

Also known as trichonocardiasis and leptothrix, this fungoid disease of hairs, affecting chiefly the axillæ, is very common amongst soldiers in the tropics (Plate 33). Occasionally the pubic hairs are affected, but, unless irritation of the skin develops, the infection is usually unnoticed, and hence its spread is facilitated. When the skin becomes inflamed, the disease is a cause of inefficiency.

Etiology.—The disease is usually caused by *Actinomyces tenuis* (Castellani, 1912), which is a fungus having the ability to form a resistant, horn-like glue. On examining an infected hair microscopically under the low power, irregular rounded formations of a yellowish colour are seen; these partially or totally encircle the shaft. Under the high power these formations are seen to be collections of mycelial hyphæ embedded in an amorphous cement. In some cases the concretions are black in colour, due to the presence of *Micrococcus nigrescens* (Castellani, 1911), which probably can live in symbiosis with the fungus; in other instances the concretions may be red, due tothe presence of *Micrococcus* (*rhodococcus*) *castellanii* (Chalmers and Farell, 1915).

Actinomyces sendaiensis (Ping Ting Huang, 1933), which, in pure culture, is black in colour, has been isolated from twenty-five cases of trichomycosis.

Symptoms.—The incubation period is from two weeks upwards. Both axillary and pubic hairs may be affected, or either separately. Clinically, as indicated by the etiology, there are three types, Trichomycosis flava, T. nigra and T. rubra. The hairs are seen to have a coated, beaded or nodular appearance, and the deposit on them is either black, yellow or red (Plate 34). The affected hairs break easily. The adjacent skin may be affected and may be reddened or show a yellow discoloration.

Prophylaxis.—Keep the axillæ shaved. As is well known, nearly all the natives of tropical countries shave the axillæ, and it would be a good thing if Europeans did likewise. Failing this, dusting with a mixture of powdered sulphur and fuller's earth is useful. Frequent changes of underclothing and bathing the parts liable to infection are helpful measures.

Treatment.—Shave the affected areas and apply either ung. hyd. ammon. dil. or sulphur ointment. Frequent applications of 1/1000 lot. hyd. perchlor. or 1/3000 formalin solution are alternative measures. If the skin is inflamed use calamine lotion for a few days before employing stronger remedies.

In resistant cases, bathe the parts twice daily with a lotion containing 1 drachm of formalin in 6 ounces of rectified spirit, and apply 2 per cent. sulphur ointment at night.

The affected areas should be kept shaved for a period of four to eight weeks.

TUNGIASIS

The sand-flea *Tunga* penetrans*, the chigger, jigger or chigoe was a veritable pest in the East African campaign of the last war. Native troops and carriers, being well acquainted with it, usually deal promptly with it, but to many of the Indian troops it came as a new experience, and now and again neglected cases of chigger infection occurred. It was certainly a cause of inefficiency.

Etiology.—The insect (Plate 35, A) is rather like the common flea but smaller. It is red or reddish-brown in colour, and very active. Males and females live in dry sandy soil and suck the blood of all warm-blooded animals, especially pigs. After impregnation the female burrows diagonally into the skin of a mammal or bird, and, nourished by blood, proceeds to ovulation. Her abdomen distends enormously until, when full of ripe eggs, it is as big as a small pea (Plate 35, B and C). The eggs escape through the skin opening, hatch into larvæ, which spin cocoons from which in eight or ten days the fleas emerge.

Symptoms.—The feet are the parts most commonly infested, and chiggers are common between the toes and under the toe-nails. As troops often sleep on the ground, other regions are often affected. As a rule, only one or two chiggers are found at a time, but large numbers may be present. Indeed, the sole of a foot may be honeycombed with them.

Itching and irritation lead to examination of the affected part, and a little dark dot is noted. This is caused by the last two abdominal segments presenting at the skin orifice, for the female flea lies head inwards in her burrow. Unless she is removed pus forms round the distended abdomen and the skin becomes inflamed, raised and swollen. In the middle of the little tumour so formed is a depression with the black dot (end of abdomen) at its centre. Once the eggs are discharged the skin ulcerates and the chigger is expelled. A small sore is left, which is very liable to infection with septic organisms and even with tetanus. Neglected sores accord-

* *Tunga* Jaroki, 1838 = *Dermatophilus* Lucas, 1839.

ingly go from bad to worse, and the ravages of chiggers in cases of multiple infection may be very severe and lead to death from secondary causes.

Prophylaxis.—Whenever possible, camps should not be formed in chigger-infested localities. Hence the neighbourhood of native villages should be avoided. The ground should be swept and, if necessary, fired. The floors of tents and huts may be sprinkled with insecticide. Flaked naphthalene is good, or a strong infusion of native tobacco. The latter may be used inside boots and shoes. Walking barefoot, and sleeping unprotected on the ground, should be avoided. A daily foot parade should be instituted and strict attention paid to the cleanliness of the feet. The following method of preventing the chigger gaining entrance to the skin is recommended as one which merits a good trial :—

Wash the feet thoroughly and then rub in a mixture consisting of 5 drops of liquor cresoli saponatus in 1 ounce of vaseline. Special care should be taken to treat in this way the spaces between the toes and the under-surface of the toes. It is said that this method will afford protection for three days. It has also the advantage that any chiggers which have penetrated the skin before its application are killed and can be more easily and painlessly extracted than when alive.

Treatment.—It is well to employ some expert natives for removing the chiggers. Long practice enables them to obtain the best results. The infected part is bathed with an antiseptic lotion, and the little operation consists in widening the skin orifice with a sharp, clean needle, and freeing the chigger from the surrounding tissues in order to enucleate it whole. Then clean and dress the resulting lesion. If the chigger is ruptured it has to be removed by the aid of forceps, and this complicates matters and is a more painful procedure.

SLEEPING SICKNESS

Trypanosomiasis is endemic over about a quarter of the African continent, and in epidemic form has sometimes depopulated large areas. Before the present war about a million natives were treated for it every year. In West Africa, where it ranges from Senegal in the north to Angola in the south, over 70,000 cases were recorded in British hospitals in 1936, in which year 60,000 were treated in Nigeria alone. Inland, it extends to Timbuctoo and Lake Chad, the southern Sudan, Lake Victoria, Lake Tanganyika and Rhodesia.

A form of sleeping sickness known as Chagas' Disease is prevalent amongst infants and young children in South America. The causal organism is a trypanosome, *Trypanosoma cruzi*, and is transmitted by species of reduviid bugs of the genus, *Triatoma*.

Etiology.—Sleeping sickness is the terminal stage of human trypanosomiasis, and there are in Africa two distinct clinical forms of the latter. The trypanosomiasis of the Belgian Congo, Uganda and Tanganyika Territory often runs a relatively benign course with little to indicate its presence beyond the palpable glands.

This variety due to *Trypanosoma gambiense* (Plate 13) is carried mainly by two species of tsetse fly, *Glossina palpalis* (Plate 4) and *G. tachinoides*. Trypanosomiasis as found in Nyasaland and Rhodesia, due to *T. rhodesiense* (Plate 14), is a much more serious problem and a high proportion of those attacked develop the classical mental and neurological symptoms characteristic of the disease, from which they usually die, often within a relatively short time, unless diagnosed and treated energetically early in the course of the disease. The vectors of this variety are *G. morsitans* (Plate 3), and *G. swynnertoni*.

Many authorities, Kleine amongst them, consider *T. rhodesiense* and *T. gambiense* to be the same species with different degrees of virulence, whilst many also consider that *T. rhodesiense* and *T. brucei*, which causes " nagana " in animals, are identical.

The tsetse fly acts as a true intermediate host of the trypanosome it transmits. It is not merely a mechanical vector. In all probability the lymphatic system is quite as important a habitat of the trypanosomes as is the blood. The parasites produce a toxin to which in part the symptoms are due. The incubation period in man is not definitely known. It is probably about three weeks.

Symptoms.—The fly bite causes a slight local irritation which soon subsides, and a little later the disease begins insidiously with an irregular, intermittent fever which may be accompanied by a curious, patchy erythema, best seen on white skins. It is sometimes annular and is of a fleeting nature. Localized œdema may appear and hyperæsthesia be present. Cardiac excitability may be noticed and slight splenic enlargement. The fever subsides only to recur, it may be after a long interval. Gradually the patient grows weaker, he suffers from headache, his cervical glands and other lymphatic glands begin to enlarge and may be tender. At first soft, they become indurated later. The blood shows slight anæmia. In some cases the spleen becomes very large and the liver may increase in size. This is the first stage, that of trypanosome fever, and it may end in recovery. More commonly the cerebral stage, that of sleeping sickness, develops, but it may not make its appearance for years. Usually it occurs in from four to eight months. It may commence with acute, even maniacal symptoms, but as a rule there is merely an increase of the weakness and languor. The patient becomes dull and disinclined for exertion, he walks slowly and has a shuffling gait. His face gets puffy and wears a sulky or vacant expression. He becomes drowsy, exhibits tremors of various kinds and suffers from a dull headache, which at times, however, is very severe. He still has fever, the temperature running up at nights, and ere long he becomes a hopeless invalid, lying helpless and indifferent to his surroundings though still capable of being roused and of speaking and swallowing. Still later he will fall asleep with half-masticated food in his mouth, and as time goes on he loses flesh, the tremors increase, he is seized with convulsions, his neck muscles may become rigid and his head retracted, so much so that, at this stage, the condition may be mistaken for cerebro-spinal fever. Trophic changes set in, there may be paralysis, the lips become swollen and saliva dribbles from

the mouth. Incontinence of urine and fæces sets in, and if an intercurrent affection such as pneumonia or dysentery does not terminate the scene, the patient becomes comatose before the end or dies of exhaustion.

The severe nervous symptoms coincide with the entry of the trypanosomes into the cerebro-spinal system.

The form due to *T. rhodesiense* runs a more rapid course than Uganda sleeping sickness and appears to be almost invariably fatal unless treated energetically in the early stage. Very often there is no enlargement of cervical glands.

Diagnosis.—During the first stage this depends chiefly on the discovery of the causative parasites in the peripheral blood or the cervical gland juice. They are not, as a rule, numerous in either. In the cerebral stage the trypanosomes can still be found in the blood, often in large numbers at the pre-agonal period, and they are also present in the cerebro-spinal fluid and can usually be found after centrifugation. Recently, the causal trypanosome has been found in material removed by sternal puncture.

Inoculation of a susceptible animal, such as a monkey (*Cercopithecus*), dog, or guinea-pig, is often a great aid in diagnosis, and this method may also be used to test the efficacy of treatment.

It must be understood that large numbers of trypanosomes may be present in the brain and yet absent from the blood and cerebro-spinal fluid when examined microscopically or tested by animal inoculation. Therefore such negative findings cannot be taken as absolute proof of freedom from trypanosomiasis, whether the tests are employed as a diagnostic measure, or as a control in treatment.

Differential Diagnosis.—Malaria, kala-azar, some forms of cerebral syphilis, especially general paralysis, and pellagra may be mentioned as diseases from which trypanosome fever and sleeping sickness must be distinguished.

The serum-aldehyde test introduce by Napier for the diagnosis of kala-azar has given positive results in a high proportion of individuals suffering from trypanosomiasis.

Prophylaxis.—General prophylaxis is too large a subject for consideration here. It involves amongst other matters the question of the rôle of big game as reservoirs of infection. Personal prophylaxis consists in protecting against the bites of tsetse flies (*see* p. 48). A single dose of a curative drug such as Antrypol may give a few months' protection.

Treatment.—The most effective drugs in the early stages are certain complex urea preparations, of which the best known are Bayer 205 (Germanin*), the French drug 309 (Moranyl), first synthesized by Fourneau, and the British Antrypol (B.D.H.). These may be administered intravenously in 1 gramme doses dissolved in 10 c.cm. of distilled water, the injections being given once a week. A total of 10 g. may effect a cure.

Experience shows that better results may be obtained by giving the first three doses more closely spaced, say on the 1st, 3rd, and 5th days, the subsequent doses being given weekly. There is some doubt as to whether there is any advantage in continuing the course

---

* British equivalent—Suramin.

beyond three doses, for it appears that the beneficial effects, which are often most striking in early cases, are due to the initial injections.

Bayer 205 has been given subcutaneously, 1 g. in 5 c.cm. of saline, but the injections are apt to be painful.

As this preparation may give rise to albuminuria, the urine must be watched carefully during treatment. If this complication should unfortunately occur, it does not necessarily contra-indicate further treatment.

Where there is evidence of involvement of the central nervous system, tryparsamide, an arsenical preparation which is administered intravenously, holds out the greatest hope of benefit. Commence with 1 g. in 10 c.cm. of distilled water, and continue with a dose of 2 g. once a week until twelve doses have been given. In the case of a patient who has already been treated vigorously with arsenic, it is better to employ Bayer 205 instead of tryparsamide, for the parasites may have become arsenic-fast, and, moreover, there is a danger that the further administration of an arsenical preparation may give rise to ocular changes.

Recent work by York suggests that diamidines may be of use in the treatment of trypanosomiasis.

Prior to the introduction of these newer preparations it was usual to treat trypanosomiasis by alternating courses of tartar emetic intravenously, and Atoxyl* intramuscularly. If this line of treatment is adopted for any reason, give bi-weekly injections of antimony, ½–2 grains, for about thirty doses. Then continue with atoxyl for two or three months, using a 10 per cent. solution in normal saline freshly prepared and free from precipitate. Not more than 7 or 8 grains should be injected at a time, say one dose every fifth day, or 3 grains every third day. Then revert to antimony, and ring the changes in this way for at least two years, stopping the atoxyl only if symptoms of arsenical poisoning supervene.

SMALL-POX

It is not intended to deal with small-pox in quite the same manner as other diseases are treated in these Memoranda. Aberrant forms of small-pox occur in the tropics, such as the so-called Amaas or Kaffir milk-pox, as Alastrim is termed in Africa. This is very like a mild variola, but some think that it is a distinct disease. It differs from classical small-pox chiefly in its low mortality and its limited epidemic spread. It appears to breed true. Although rarely fatal, it may have at the outset a sharp and severe fever like variola, of which it is probably a minor form.

The medical officer should always bear in mind the possibility of small-pox, and be suspicious of a disease commencing with a chill and continuing with high fever, severe headache, severe pains in the back and vomiting. He should remember that the broad features of the small-pox rash are that " it prefers the upper half of the body to the lower, that it is a rash of the face and arms rather

---

* British equivalent—Sodium arsanilate.

than of the trunk and legs, that it is a rash of the distal ends of the limbs rather than of the proximal, of the back of the trunk rather than of the front, of extensor surfaces rather than of flexor, and that it is a rash which shuns the most pronounced flexures" (Ricketts and Byles).

One of the chief difficulties which arises is to decide whether a case is variola or varicella, and the difficulty is apt to be greater when dealing with a dark skin. There is no single characteristic sign on which absolute reliance can be placed, and it is often extremely difficult to distinguish moderately severe chicken-pox from mild small-pox. Under war conditions it is well invariably to vaccinate and regard the condition as small-pox.

It is always helpful to mark out an area, the so-called skin window, and observe the character of the rash within it, whether the eruption is all more or less at one stage as in variola or there is evidence of successive crops as in varicella.

The following remarks by Thomas are likely to prove helpful. He says that "the greater depth of the initial skin lesion in small-pox explains :—

(1) The shotty character of the rash; (2) the pearly-yellow contents of the vesicle, the colour being due to the thicker epithelial covering; (3) the hardness and hemispherical surface of the vesicle; (4) the absence of the crenated edge in the vesicle. This is possibly damped out by the thicker layer of epithelium, just as the several layers of an onion hide the irregularities at the core; (5) the absence of early cupped scabs owing to the difficulty of rupture; (6) the pitting; (7) the thickness of the crusts; (8) the presence of 'seeds' in the palms and soles; (9) possibly the umbilication and the formation of septa."

"The superficial position of the lesion in chicken-pox explains :—(1) the moderately soft character of the rash; (2) the clear transparent, almost colourless contents of the vesicle, due to the very thin epithelial covering; (3) the soft and sometimes spherical or ellipsoidal surface of the vesicle; (4) presence of crenation or puckering in the vesicle; (5) early cupped scabs; (6) the absence of pitting, save in severe cases; (7) the thinness of the crusts; (8) the absence of "seeds" in palms and soles."

By far the most important feature of the rash in diagnosis is its *distribution*, which has been already described.

It must be remembered, especially when dealing with natives, that certain aspects of syphilis have to be distinguished from small-pox, which at times they may rather closely resemble. Careful inquiry and inspection usually clear up the diagnosis. If possible in doubtful cases the reaction of a sensitized rabbit to vaccination with pock contents should be observed.

Treatment.—There is good evidence that a 5 per cent. solution of permanganate of potash painted on the skin of small-pox cases, or used as a bath, mitigates the severity of the disease, and also lessens the risk of infection.

Vaccination.*—The usual faults in technique are lack of cleanliness causing sepsis, the use of too strong an antiseptic for cleansing

* *See* Appendix 18, Regulations for the Medical Services of the Army, 1938.

the skin (soap and water and a nail brush, followed by a rub with alcohol, meet the case), overheating of the lancet needle or scarifier when sterilizing it, drawing blood, exposure of the recently vaccinated area to the hot sun (a very important point in the tropics), charring of the lymph in the capillary tube when sealing.

There should be one linear incision of ¼ inch in length, and the total area of vesicle formation should not be less than half a square inch. Cross hatching should not be employed. The following is Rosenau's account of the course of the eruption which follows successful vaccination, and it is certainly a comment on the way this important preventive measure is taught at some of our Schools of Medicine that it is thought necessary to include it here.

"The primary wound soon heals. Apparently nothing occurs for 3 to 4 days, which is the period of incubation. Then one or more small papules appear upon the skin where the vaccine virus was introduced. The papule is small, round, flat, bright red, hard, but superficial. About the fifth day the summit of the papule becomes vesicular. The vesicle is at first clear and pearl-like. Umbilication soon develops as the vesicle enlarges. A deep, red, and swollen areola surrounds the vesicle and grows wider as the lesion advances. This gives the picture of the 'pearl upon the rose leaf' which constitutes the true Jennerian vesicle. By the seventh day the vesicle is full size, round or oval, flat on top, umbilicated, and contents clear. It is multilocular; if pricked with a pin or accidentally opened only that portion of the lymph contained in the compartment opened will exude. By the eighth day it turns yellowish, the middle is fuller, following which the so-called second umbilication develops. Meanwhile the areola deepens, widens, and may be swollen. The skin feels hot, is painful, and the axillary glands become enlarged and tender. About the ninth day the areola begins to fade and the swelling subsides. By the eleventh or twelfth day the vesicle rapidly dries, leaving a brown, wrinkled scab, which finally drops off. It should never be removed, as it forms the best bandage.

"The scar is at first red, finally white, with the pits or foveations so characteristic of true cowpox."

A practical point of some importance is to see that the vaccinee does not deliberately remove the vaccine lymph after vaccination. A tragic case is on record in Egypt where a soldier did so, licking off the lymph with his tongue. Not long afterwards he developed a severe attack of small-pox and died of the disease.

Subcutaneous vaccination is in vogue in many countries, but little use is made of it in military practice in this country.

SPRUE

In the East sprue is common in South China, the East Indies, Idia and Ceylon, and in the West, the West Indies and the Southern United States. For some reason so far unexplained, the disease is rare in Tropical Africa. Usually it affects those who have been long resident in endemic centres, but newcomers are not necessarily exempt from attack.

Etiology.—The cause of sprue is unknown. Hamilton Fairley attributes the disease to a metabolic breakdown of the gastro-intestinal tract of unknown etiology and considers infection to be an unlikely cause. The view that the responsible agent is a yeast has been generally abandoned, though it is possible that some part of the intestinal symptoms may be due to invading fungi, and it must be admitted that certain etiological factors connected with the disease fit in well with the theory of a chronic intestinal infection in some way connected with a warm humid climate.

H. H. Scott noted the incidence of tetany in many cases of sprue and advanced a theory of parathyroid deficiency with resulting hypocalcæmia. Consequently, he advised parathyroid tablets and calcium as part of the treatment. It is now realized that the hypocalcæmia with resulting tetany is due to malabsorption of calcium and *not* to parathyroid dysfunction.

Other theories are that a vitamin deficiency is to blame, a view that gains some support from feeding experiments on animals, but appears unacceptable in many instances as the individuals attacked have been shown to have had a diet entirely adequate in its vitamin content; and that sprue is a sequel of amœbic or of bacillary dysentery. It seems possible that the early symptoms have a partly physiological basis, and indicate an attempt by the body to re-establish a metabolic balance which has been disturbed by adverse climatic conditions. The struggle continues under increasing handicaps, leading to glandular exhaustion and deficiency, and to toxic atrophy of the intestinal tract. However this may be, sprue is in some way associated with a combination of atmospheric humidity and heat, although it must be remembered that the disease is unknown in many districts where adverse climatic conditions of the type mentioned prevail. This suggests something more than climate and debility as the root cause of the syndrome, and some chronic infection, maybe of virus origin, may even yet prove to be responsible.

A disturbance in liver function appears to be responsible for the earlier symptoms, while the late starvation signs are accounted for, in some cases at least, by degenerative changes affecting the intestinal villi and glands. In other, apparently typical cases, no such degenerative lesions are found at autopsy and the cause of the wasting is obscure. Fat absorption is markedly diminished and some think there is an actual excretion of fat from the body.

Symptoms and Morbid Anatomy

Symptoms at Onset.—In at least several of the endemic areas there is a form of diarrhœa common during the hot humid season, and seemingly quite distinct from mild dysentery. The diarrhœa is usually accompanied by some digestive disturbance and perhaps flatulence, and is characterized by periods of remission and recrudescence. The stools tend to show some loss of colour. In localities where there is marked seasonal change, the onset of cool dry weather may check in a few days a diarrhœa that has lasted off and on for several months, or a short sea voyage may have the same

effect. In the majority of cases such a diarrhœa gradually passes off, or at least is tolerated, but in some small proportion the condition progresses, the symptoms becoming more sprue-like, until finally typical sprue supervenes. Even when a sprue patient fixes the commencement of his symptoms at some definite time, a cross-examination will often bring out a history of dyspepsia and looseness of the bowels antedating the supposed onset by months or years.

In other instances sprue follows dysentery, either bacillary or amœbic, and if the latter, amœbæ may be found in the typical sprue stools. The sequence of sprue on hill diarrhœa is so frequent as to suggest some etiological relationship between the two conditions. Again, the onset may be acute, and an attack of what seemed to be a simple diarrhœa quickly assumes the characteristic features of sprue. In yet other cases emaciation without other complaint may be the presenting symptom. Soldiers may sometimes be picked out on a routine parade on account of their obvious emaciation, who stoutly deny that there is anything whatsoever wrong with their health, although they may have lost several stone in weight in as many weeks. Subsequent investigation of these individuals has, however, shown them to have been suffering from typical sprue, and one wonders how they could have carried on so long without complaint or apparent inconvenience. Emaciation without corresponding debility is characteristic of at least one type of sprue in its early stages. Cases of this type usually do well on a regulated simple sprue diet and may not even have to leave the endemic area.

Symptoms of Established Disease.—These symptoms are best considered in groups. *Stomach and Intestine.*—The patient complains of indigestion, and of flatulence affecting both the stomach and intestine as evidenced by eructations, borborygmi and distension. In advanced cases the feeling of abdominal tension may be so severe as to incapacitate the sufferer until the gas can be expelled. There is looseness of the bowels, usually not of a marked degree, two or three motions being passed during the morning, and perhaps no more for the rest of the day. The motions, especially the first in the day, are often passed with explosive violence, and the call to stool may be sudden and imperative. Occasionally diarrhœa is more marked, and pale, watery, bubbly stools are passed every couple of hours or so throughout the day. Any pre-existing anal trouble, such as hæmorrhoids or fissure, tends to become aggravated, and may constitute the patient's chief complaint. Typically the stools are pultaceous, light coloured or white, foul-smelling and blown out with gas. Fermentation is so active that if a specimen is left in a corked tube, the cork may be found later blown out. They are very bulky, so that the patient may wonder how with so small an intake he can pass so much. The total fat in normal fæces is under 25 per cent. of the dry weight, often much lower, but in sprue it is increased to 30, 50, 60 per cent. or more. Typically the fatty acids are increased in proportion to the neutral fat, N.F. 1 : F.A. 3 to 5, instead of the normal N.F. 1 : F.A. 2. In pancreatic disease the ratio may be N.F. 15 : F.A. 1, owing to defective fat-splitting (Thompson). The results of fat analysis, however, are subject to

variation depending on the rate of passage of food through the intestinal canal, the time that elapses before the specimen is examined, and the effect of heat if the material is dried by this method, so that otherwise typical cases of sprue, which react at once to treatment, may not show the fatty constituents present in the proportion stated.

Mouth.—There is thinning of the mucous membrane of the mouth and tongue, with patches of congestion, vesicles, and small superficial ulcers. These are seen on the tip, edges, and under surface of the tongue, inside the lips and cheeks, and sometimes on the palate and in the throat. The lesions tend to appear in crops, and may render mastication an agony to the patient. The accompanying irritation leads to increased salivation and sometimes actual dribbling. There may be areas of superficial erosion, most easily seen if the tongue is protruded and allowed to dry, when glistening patches not otherwise apparent are easily detected. The surface of the tongue may look red, raw, and shiny, and resemble a raw beefsteak in appearance. It is smooth owing to atrophy of the filiform papillæ, while the fungiform papillæ may stand out red and enlarged. Especially in chronic cases the surface of the tongue may show the presence of fissures. In spite of the dyspepsia it remains clean.

Mouth symptoms may be a very early feature, and a patient who shows little else wrong may complain that certain pungent articles of diet " sting " his tongue. On the other hand, a sore mouth may suddenly develop after two or three years of otherwise typical sprue. And again, the disease may run its whole course without lesions in the mouth.

Blood.—Some degree of anæmia is present in established sprue, and a red cell count of 3½ million or 4 million per c.mm. would be an average finding in a case of moderate severity. In severe cases the blood picture may approach that of pernicious anæmia, with megalocytes, normoblasts, and a high colour index. Megaloblastic hyperplasia of the bone marrow is often seen in severe cases. If the morbid process continues in a severe enough form, the bone marrow undergoes toxic degenerative changes, including even complete aplasia, with a resulting fatal aplastic anæmia, characterized by a falling red cell count, and no sign in the peripheral blood of attempted regeneration. It is always a grave sign if anæmia increases after the gastro-intestinal symptoms have definitely improved.

The white cell count shows some reduction, but not an actual leucopenia unless the anæmia is very severe. There is a relative increase of lymphocytes at the expense of the polymorphonuclear cells.

Mental Changes.—In proportion to the severity and duration of the illness mental deterioration is present, often not obvious to the patients themselves, but noticed by their friends or fellow workers. Lack of concentration, infirmity of purpose, depression, irritability and unreasonableness may be in evidence. They are slow in answering questions which require thought, but once under way

they may be tryingly garrulous. They are introspective, and, if persons of intelligence, delight in analysing their symptoms and may be full of knowledge, of a sort, regarding sprue.

General.—There is increasing loss of weight, and in advanced cases the sufferer may be reduced to the classical condition of a skeleton with a blown-out abdomen. The organs share in the general wasting, so that the area of liver dullness is much decreased. The temperature is subnormal and the patient abnormally sensitive to cold, and in some cases cramps and even tetany may occur. The skin is pigmented, especially that of the face and forehead. Generalized œdema may mask the loss of flesh.

Toxic peripheral neuritis with sensory changes is a not uncommon complication of long-standing sprue, especially if accompanied by severe anæmia. In those cases in which the anæmia is macrocytic in type the differential diagnosis from subacute combined degeneration of the cord may present real difficulties.

If not checked by treatment the disease drags on its weary course, interrupted by temporary remissions which are followed by relapse ; wasting and debility increase, and the patient dies of starvation, anæmia, or some intercurrent disease.

Morbid Anatomy.—The most characteristic changes are found in the intestinal mucosa which shows areas of thinning, rarely accompanied by ulceration ; this being part of the general wasting process and not a necessary part of the sprue syndrome. The villi and glands are involved in the degenerative process, and the villi affected appear shrivelled, or may undergo complete atrophy and replacement by cicatricial tissue. The muscular coat is also atrophied. The erosions of the mucous membrane may be present throughout the alimentary tract, more or less generally, or in patches, or restricted to some part. In some apparently typical cases, however, no obvious intestinal changes are seen post mortem.

The bone marrow shows characteristic changes. In many cases the interior of the long bones is filled with red marrow and there is a megaloblastic hyperplasia. A peculiar gelatinous appearance of the yellow marrow, also seen in other intestinal diseases, is said to be characteristic. The liver, spleen, and kidneys often give the Prussian blue reaction due to the deposition of hæmosiderin.

Diagnosis and Prognosis

Diagnosis.—The combination of flatulent dyspepsia, pale frothy stools, sore mouth, and loss of weight, often extreme, presents an unmistakable picture, but this diagnostic tetrad may not be complete, and diagnosis and treatment should never be postponed because, for instance, mouth lesions are absent, or there has been no serious loss of weight. Larval sprue is a common and widespread condition and often escapes detection. The subject may complain only of some dyspepsia and flatulence, and perhaps is found to pass one or two pultaceous stools daily. If these show any loss of colour, or if the total fat is increased, the patient, however mild the symptoms, should be confined to bed, thoroughly investigated and

put on a sprue diet if the investigation warrants it. A speedy response encourages persistence with the treatment. Do not handicap him in his career by making an official diagnosis of sprue if this is reasonably in doubt, but never postpone or withhold treatment on this account. Many persons suffering from classical sprue give a history of mild symptoms, like those mentioned, which persisted undiagnosed for months or years before progressing to the text-book picture.

Differential Diagnosis.—The result of chemical analysis of the fæces is usually helpful in distinguishing between chronic pancreatitis and sprue. In the former there is defective splitting of fats, while in sprue the process goes on actively, even to excess. Pancreatitis does not give rise to mouth symptoms, nor does the disease react to dietetic treatment in the striking manner common in sprue. The intestinal symptoms of pellagra may resemble those of sprue, but the development of erythema of the face and hands will prevent confusion. The history of the case, the later development of severe anæmia, and the usual absence of megaloblasts will distinguish from pernicious anæmia. Hill diarrhœa that does not clear up should be regarded as sprue.

Prognosis.—The age of the patient and the duration of the disease are important factors. Young adults as a rule respond more readily to treatment than persons past middle age. The earlier a patient comes under treatment the more hopeful is the prospect, for in cases of long standing the intestine may have suffered irreparable damage with destruction of villi and glands. Persisting anæmia of a severe grade is a grave complication, for it is evidence of hypoplasia of the bone marrow with the ever-present danger of the development of aplastic anæmia.

When treatment has effected a clinical cure, the ultimate prognosis is affected in a large degree by economic considerations. If circumstances permit of such persons remaining at home, the position is very hopeful. On the other hand, if they must return to an endemic area, the danger of relapse is greatly increased. Certainly anyone who relapses after apparent recovery ought never to go abroad again. No period of freedom from symptoms can be laid down as necessarily indicating a cure, for the disease may recur after years of seemingly perfect health.

Treatment

Whatever procedure he decides to adopt, the medical officer must gain the patient's confidence and respect, and consistently refuse to deviate from the chosen regimen through any whim of the patient or his friends. The prime necessity is, of course, that the medical officer should have confidence in himself. Make the objects of the treatment clear to the patient and his immediate relatives. Explain that, owing to the inflamed state of the intestine, only a small quantity of food can be absorbed, so that anything eaten in excess of this amount only ferments and increases the damage already done. The mouth lesions if present, can be pointed out as illustrating the condition of the alimentary tract. Explanations along these lines

are gratefully received, and in most instances prevent future misunderstanding and dread of " starvation."

Rest in bed and warmth are essential. Every stool, unless the number is excessive, must be kept until seen by the medical officer; in this way alone can progress be estimated satisfactorily, and the diet regulated. The most encouraging sign of improvement, and one to be watched for unceasingly, is a return of colour to the stools. Usually this is first apparent as a localized brownish patch, followed later by a more diffuse light yellow tinge which gradually darkens from day to day, and becomes brown. Even if the stools are small and well formed, do not be satisfied with the patient's condition until the colour is restored.

When a patient who has made satisfactory progress suddenly passes a foul and loose stool for no apparent reason and without any premonitory dyspepsia or flatulence to suggest a commencing relapse, always suspect that food has been smuggled in, and take such measures as are indicated. The subterfuges and trickery to which a seemingly sensible patient may resort in order to satisfy a craving for currant cake or pork pies must be experienced to be believed. In three separate instances where the writer suspected irregularities of this kind, but where there was at the time no direct evidence, he tried to warn the supposed offenders by introducing in ordinary conversation an account of patients who had endangered their lives in this way. The suspects all expressed horror and indignation at such criminal foolishness and ingratitude. None the less each of them was caught later *in flagrante delicto*. Fortunately such patients represent only a very small part of the whole, but for that reason they are the more likely to escape suspicion. One can attribute their behaviour only to mental deterioration resulting from the disease.

Many lines of treatment have been employed with benefit in sprue, but it is certain that no rule-of-thumb procedure will meet every case. A patient who does badly on milk may react at once when placed on a diet of meat juice and underdone meat, and *vice versa*. Whatever regimen is adopted, scrupulous attention to minutiæ is essential to success, for it is a common experience that a patient who fails to benefit in hospital A, may progress rapidly in hospital B on a diet nominally the same.

The milk cure is widely used. In this the patient commences with three pints of milk in the twenty-four hours, and this quantity is slowly increased until he is taking six or seven pints a day. No other food is permitted until the stools have been solid for six weeks. Particulars of this treatment, and many others, will be found in standard text-books. Here it is proposed only to give details of the treatment which has been employed, with various modifications, in Millbank for many years, for it has proved more satisfactory there than any other that has been tried. The basis of the procedure is administration of milk, vitamins of fresh fruit and yeast, liver products and later liver. The diet progresses by four-day gradations, not more than one addition being made at a time. *All milk must be taken with a teaspoon.* The dietary treatment is prefaced by a dose of castor oil sufficient to clear out the fermenting material, but avoiding a severe purge. The commencing diets shown below

will be found successful in the great majority of cases. It is not claimed that the various special preparations employed are specific, and doubtless other substances would prove equally effective. In these diets liver extract replaces the hepatopopson formerly included.

The aim is to build up by degrees the three customary meals of the day, and therefore the more substantial additions to the diet are made at appropriate hours, and the intervening feeds gradually dropped. Eggs are first added raw and beaten up in a milk feed. Chicken liver (4 oz. steamed, passed through a fine sieve, and indigestible matter removed) is added about the twenty-fourth day. This is then increased to 8 oz., and about the fortieth day is replaced by sheep or calves' liver prepared in the same way.

In passing to a normal diet, beef is added first as underdone steak, and bread in the form of thin slices of wholemeal toast.

Within two or three days of commencing treatment, an appreciable improvement in digestion with diminished gas formation may be expected ; before long the stools become smaller and formed, and later the colour begins to return. If there is any tendency to constipation, secure a daily motion by the use of liquid paraffin, bearing in mind that this medicament (or any other soluble in ether) will appear as fat if a fæcal analysis is made.

The rate of progression in the diet is regulated by the state of the stools, and not more than one untested addition must be made at a time, in small amount only, and increased later if there is no sign of intolerance. As a rule a patient looks forward eagerly to his meals, but if he should be disinclined to eat do not overtax the digestion, but miss out one or two of the less essential feeds until the appetite returns.

If milk is not well digested in spite of being taken with a teaspoon, give it diluted or citrated. If it is still found to disagree after a fair trial, replace by Benger's food or junket. Some patients who are unable to tolerate a milk diet indefinitely, do well if milk is stopped regularly for a few days, and a diet of meat juice and underdone meat substituted during the intermission.

Hamilton Fairley recommends a dietary with a high protein, low fat and carbohydrate content. To achieve this he makes use of two alternative dietaries, either of which can be given from the commencement of treatment.

The first, especially useful in the case of those unable to tolerate milk or its products, includes high-grade protein in the shape of lean rump steak, lightly cooked for a few minutes only, and served hot. Commencing with 3 oz. of this he works up to 7 oz. Other items of relatively low food value but with a high vitamin content are added cautiously and progressively.

The second alternative dietary has Sprulac, an artificially prepared milk product of high protein and low fat and carbohydrate content, as its principal constituent.

For further details of these high protein diets, which have proved extremely successful in very many hands, Fairley's original papers should be consulted.

Most experts agree that liver in some form plays an important part in the treatment of sprue, especially when anæmia of a megalocytic type threatens. It has been shown that the more highly

purified liver extracts such as anahæmin, which have given satisfactory results in the treatment of pernicious anæmia, are relatively ineffective in the treatment of the nutritional anæmia of the East, including tropical sprue. Less highly purified liver extracts should therefore be used.

Usually it is sufficient to give liver extract by mouth, but in some cases, especially at the outset and if severe, absorption by this route appears to be defective and recourse must be had to parenteral injections of such products as Campolon, Hepostab, or Pernæmon forte, for the first ten days or so.

The usual type of secondary anæmia found in sprue requires no special treatment. If it is of a more severe grade, massive iron therapy may be employed, and if the blood picture indicates an anæmia of a pernicious type, blood transfusion must be resorted to and repeated as required.

Arising out of the supposed analogy between sprue and pellagra nicotinic acid, admittedly efficacious in the treatment of the latter disease, has been used with varying success in the former.

In sprue the gastric HCl may be increased, normal in amount, diminished or even absent. When the disease is of long standing some degree of diminution is common, and a residual indigestion may be greatly helped by the administration of dilute hydrochloric acid. Diluted with water and orange juice, it makes a not unpleasant drink.

Dietetic Regimen

General Instructions. (i) *For the patient.*—All feeds should be taken slowly, milk and its variations, junkets and sour milk, being sipped in small quantities and retained in the mouth for an appreciable time before swallowing. Feeds may be warm or cold, as desired. Solid food should be eaten slowly and chewed thoroughly.

(ii) *For the nursing staff.*—A mouth wash is given before and after each feed.

The patient should not be roused for the 4 a.m. feed, if asleep.

Up to the time corresponding to the completion of Diet No. 8 the patient is confined to bed, but is allowed up to go to the annexes, unless the Medical Officer orders otherwise. Thereafter the patient is gradually allowed up.

1 c.cm. or 15 minims of liquor ergosterolis irradiati should be added to the day's milk in the diet. This may be measured with a hypodermic syringe.

Separate instructions may be given with regard to the administration of liver extract in cases in which :—

(*a*) It may be omitted when no anæmia is present.

(*b*) It requires to be given by injection in addition in cases showing a severe degree of anæmia.

Dilute hydrochloric acid should be given with meals when the gastric acidity is deficient. Calcium should be administered when the blood calcium is found to be low.

When Marmite is ordered with milk it may be dissolved in the milk, or given as a separate soup—1 drachm to 5 oz. of water.

Diet No. 1 (*for* 4 *days*—the rate of progression in the diet should, however, always be regulated by the state of the stool).

Time	
7.30 a.m.	Milk 8 oz.
10.00 a.m.	Milk 8 oz. Liver ext. ½ oz. on 3rd and 4th days.
1.00 p.m.	Milk 8 oz. Marmite 1 dr.
3.30 p.m.	Milk 8 oz.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 8 oz. Liver ext. ½ oz. on 3rd and 4th days.
8.00 p.m.	Milk 8 oz. Marmite 1 dr.
10.00 p.m.	Milk 10 oz.
4.00 a.m.	Milk 6 oz.

Diet No. 2 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of weak, milky tea.
8.30 a.m.	Milk 10 oz.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 8 oz. Liver ext. ½ oz.
1.00 p.m.	Milk 10 oz., or same as junket made with rennet.
3.30 p.m.	Milk 8 oz. Marmite 1 dr.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 10 oz., or junket. ½ banana mashed. Liver ext. ½ oz.
8.00 p.m.	Sour milk, or yoghourt, with sugar to taste, 8 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Diet No. 3 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of weak, milky tea.
8.30 a.m.	Milk 10 oz.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. Liver ext. ½ oz.
1.00 p.m.	Milk 10 oz., or junket. ½ banana mashed.
3.30 p.m.	Milk 10 oz. Marmite 1 dr.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 10 oz., or junket. ½ banana mashed. Liver ext. ½ oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Diet No. 4 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. Liver ext. 1 oz.

Time	
1.00 p.m.	Milk 10 oz. or same as junket. 1 banana mashed. (The banana may be served in the form of a soufflé made with the white of an egg beaten up, no sugar being used.)
3.30 p.m.	Milk 10 oz. Marmite 1 dr.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 10 oz. or same as junket. 1 banana mashed. (The banana may be served as a soufflé as at 1 p.m.) Liver ext. 1 oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Diet No. 5 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. Liver ext. 1 oz.
1.00 p.m.	Marmite soup (1 dr. to 5 oz. water). 2 or 3 small tomatoes, skinned and mashed with salt to taste. 2 bananas mashed or as soufflé with milk, 5 oz.
3.30 p.m.	Milk 10 oz.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 10 oz. or same as junket. 1 banana mashed. Liver ext. 1 oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Diet No. 6 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. 2 bananas mashed or as soufflé, with milk, 5 oz. Liver ext. 1 oz.
1.00 p.m.	Marmite soup (1dr. to 5 oz. water). 2 or 3 small tomatoes skinned and mashed, with salt to taste. Chicken liver or fish, steamed and passed through a fine sieve, 4 oz. Salt and pepper to taste. 1 rusk.
3.30 p.m.	Milk 10 oz.
4.30 p.m.	Orange juice 2 oz.
6.00 p.m.	Milk 10 oz. or same as junket. 1 banana mashed. Liver ext. 1 oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Diet No. 7 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz. with 1 raw egg beaten up in it.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. Liver ext. 1 oz.
1.00 p.m.	Marmite soup (1 dr. to 5 oz. water). 2 or 3 tomatoes, skinned and mashed, with salt to taste. Chicken liver or fish, steamed and passed through a fine sieve, 6 oz. Salt and pepper to taste. 1 rusk.
3.30 p.m.	Milk 10 oz.
4.30 p.m.	Cup of milky, weak tea.
6.00 p.m.	Calves foot jelly 2 oz. Milk 10 oz. or same as junket 1 banana mashed. Liver ext. 1 oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Orange juice not less than 2 oz. to be taken during day.

Diet No. 8 (*for* 4 *days*)

Time	
7.30 a m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz. with 1 raw egg beaten up.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
1.00 p.m.	Marmite soup (1 dr. to 5 oz. water). 2 or 3 tomatoes, skinned and mashed, with salt to taste. Underdone beef steak, lean, 4 oz. 1 rusk. 2 bananas mashed or as soufflé, with milk, 5 oz.
3.30 p.m.	Milk 10 oz.
4.30 p.m.	Cup of milky, weak tea.
6.00 p.m.	Calves foot jelly 2 oz. 1 rusk. Milk 10 oz. or same as junket, 2 bananas mashed. Liver ext. 1 oz.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 a.m.	Milk 8 oz.

Orange juice, not less than 2 oz. to be taken during day.

Diet No. 9 (*for* 4 *days*)

As in Diet No. 8, except that 1 raw egg beaten up may be added to the 3.30 p.m. feed, and ripe fruit, strawberries, skinned peaches, plums, pears or greengages ($\frac{1}{2}$ lb.) may be substituted for the bananas.

Diet No. 10 (*for* 4 *days*)

As in Diet No. 9, except that a lightly poached egg served on a rusk may be given with milk 10 oz. at 8.30 a.m., and a lightly poached egg may be served on the rusk at 6.00 p.m.

Diet No. 11 (*for* 4 *days*)

As in Diet No. 10, except that grilled, underdone beef steak served at 1.00 p.m. may be increased up to 5 oz. and the poached egg on rusk served at 6.00 p.m. may be replaced by steamed fish or chicken liver 4 oz., served on a rusk or with the same.

Diet No. 12 (*for* 4 *days*)

As in Diet No. 11, except that eggs may be lightly boiled, and two may be served at 8.30 a.m.

Diet No. 13 (*for* 4 *days*)

Time	
7.30 a.m.	Cup of milky, weak tea.
8.30 a.m.	Milk 10 oz. 1 rusk. 2 eggs, lightly boiled or poached.
10.30 a.m.	Sour milk or yoghourt, with sugar to taste, 10 oz. Liver ext. 1 oz.
1.00 p.m.	Marmite soup (1 dr. to 5 oz. water). 2 or 3 tomatoes, skinned and mashed, with salt to taste. Grilled underdone beef steak 5 oz. 1 rusk. 2 bananas, mashed or as soufflé, or other ripe fruit in season (*vide* Diet No. 9), with milk, 5 oz.
3.30 p.m.	Milk 10 oz. with 1 egg beaten up.
4.30 p.m.	Cup of milky, weak tea.
6.00 p.m.	Calves foot jelly 2 oz. Steamed fish or liver passed through a sieve, 6 oz. 1 rusk. Milk 10 oz. or same as junket. 2 bananas, or other ripe fruit in season, mashed.
8.00 p.m.	Sour milk or yoghourt, with sugar to taste, 10 oz.
10.00 p.m.	Milk 10 oz. Marmite 1 dr.
4.00 p.m.	Milk 8 oz.

Orange juice not less than 2 oz. to be placed at the bedside each day.

Diet No. 14 (*for* 4 *days*)

As in Diet No. 13, except that 2 oz. custard may be served with fruit, and boiled breast of chicken may be substituted for fish or liver at 6.00 p.m.

Diet No. 15 (*for* 4 *days*)

As in Diet No. 14, except that a thin slice of wholemeal toast may be given at 4.30 p.m.

Diet No. 16 (*for* 4 *days*)

As in Diet No. 15, except that mashed potato, 1 oz. may be substituted for rusk at 6.00 p.m. and 1.00 p.m.

Diet No. 17 (*for* 4 *days*)

As in Diet No. 16, increasing mashed potato at 1 p.m. and 6.00 p.m. to 2 oz.

Diet No. 18 (*for* 4 *days*)

As in Diet No. 17, except that wholemeal toast given at 4.30 p.m. may be lightly spread with butter.

Diet No. 19 (*for* 4 *days*)

As in Diet No. 18, except that a rusk or thin slice of toast lightly spread with butter and cream cheese (½ oz.) may be given at 6.00 p.m.

Post Sprue Diet

Articles of food allowed during convalescence and after leaving hospital.

Breakfast

Stewed fruits. Lean red meat, chop or steak.
Lightly boiled or scrambled eggs.
Fish: haddock, plaice, sole or whiting, filleted or fried, provided that the skin is discarded.
Toast or rusks. Butter in moderation; ditto jam or honey.
Weak tea made with milk and sweetened with glucose.
Fruits in season.

11.00 *a.m.*

Half pint of warm milk if desired.

Lunch

Liver soup: clear chicken or vegetable soups with liver extract.
Boiled fish. Liver cooked in various ways up to ½ lb.
Roast or boiled chicken, lean red meat, chops or steak.
Spinach, vegetable marrow, young peas or cauliflower, boiled onions, asparagus, purée of brussels sprouts.
Custard, junket, milk, jelly.
Baked apple or mashed ripe Canary banana.
Rusks or toast.
Fruits in season.
Orange juice, water and glucose.

Tea

Weak China tea, milk and glucose.
Toast with a little butter.
Wafers, water or Marie biscuits.
Madeira cake.
Sponge cakes.

Dinner (p.m.)

Liver soup.
Boiled fish, sweetbreads, kidneys, tripe, lean red meat.
Lettuce and tomato salad.
Custard, junket, baked apple with a little cream.
Toast.
Fruit jellies, calves foot jelly, and fresh fruits.

(Dinner should be the lightest meal of the day.)

Fruits Permitted

Scraped apples, papaya, oranges or orange juice.
Strawberries when in season (½ to 1 lb.).
Ripe peaches, ripe pears, hot-house grapes, ripe Canary bananas.
Bottled fruit (NOT tinned), especially peaches or pears.

Articles of Diet to be Avoided

Salmon, trout, mackerel or herrings.
Cheese.
Fresh bread.
Grease or fat, suet or milk puddings.
Nuts.
Cakes with raisins.
Starchy foods like potatoes or rice.
Pastry of all sorts.
Alcohol.
Mineral water.

As condition improves, starchy foods in the form of sago and other milk puddings and boiled potatoes in small amounts may be introduced and gradually increased, always providing that flatulence and abdominal distension are not increased. Cane sugar may also be substituted for glucose.

General Instructions.—Avoid getting over-tired, cold winds, cold or wet. Never exercise when tired, rest after lunch, go to bed early. Reside in a locality as mild as possible, preferably in a house with central heating. No cold baths or outside bathing allowed. In summer, sun bathing in moderation is often beneficial. Dinner should not be later than 7 p.m. and should be a light meal.

Recipes

1. *Liver Extract* (¼ lb. of fresh liver) added to plate of thin or thick soup at table is very satisfactory.

2. *Liver Soup.*—May also be prepared from fresh liver as follows: Take ⅞ lb. of calves liver, cut into small squares and add 1½ pints of water. Bring to the boil. Skim off all the whitish froth and simmer for 1 hour. Strain it and add one teaspoonful of marmite, well stirring all the time. Served hot.

3. *Underdone Beef.*—First-quality rump steak is selected, and all fat and skin removed. Mince with a fine mincer or scrape with a knife. Heat in dry saucepan until it becomes a greyish colour stirring vigorously all the time. This generally takes 2–3 minutes on a small gas flame. Serve immediately.

TYPHOID FEVER

Thanks chiefly to protective inoculation and in a lesser degree to efficient sanitary precautions, typhoid fever is no longer one of the chief disease factors amongst our armies in the field. As the closely allied paratyphoid fever is dealt with at some length, it is not necessary to describe fully so well-known a malady as typhoid fever.

These Memoranda will only consider such points concerning typhoid in the tropics as appear to be worthy of special attention, and in the first place it may be said that in hot countries the attack

tends to be more severe and prolonged than is the case in temperate climates (Fig. 76). As a result the mortality is often higher in the tropics and death may ensue as early as the sixth day of disease in the hypertoxic form. Degeneration of the myocardium is common and myocarditis frequently brings about a fatal issue.

In the second place the medical officer should know that unprotected men of indigenous races, whether Indian or African, are not immune from enteric infection. Indian troops undergo inoculation and so usually escape, but African troops and followers are for the most part uninoculated and so may suffer. At the same time they are much more liable to dysentery than to enteric, and it is quite possible that many possess an acquired immunity, having suffered in childhood. It is interesting to note that, in India, Gurkhas and the mounted troops have been found to be most liable to infection.

Young adult Europeans, recently arrived in the tropics or subtropics, are specially liable to infection. This is largely due to the newcomer not yet having fully undergone that complicated and indefinite but very real process known as "acclimatization"; an important item in this faulty adaptation is ignorance of how to avoid, by simple hygienic precautions, the special dangers inherent in hot climates. The chances of infection are much greater in the tropics, partly owing to the enormous prevalence of fly vectors; over-fatigue, over-exertion, and exposure to the debilitating effects of the tropical sun also act as predisposing causes.

Constipation rather than diarrhœa is the rule in tropical typhoid, and the exanthem is often absent or difficult to differentiate from the varied assortment of spots and pimples which constantly adorn the bodies of most residents in the East.

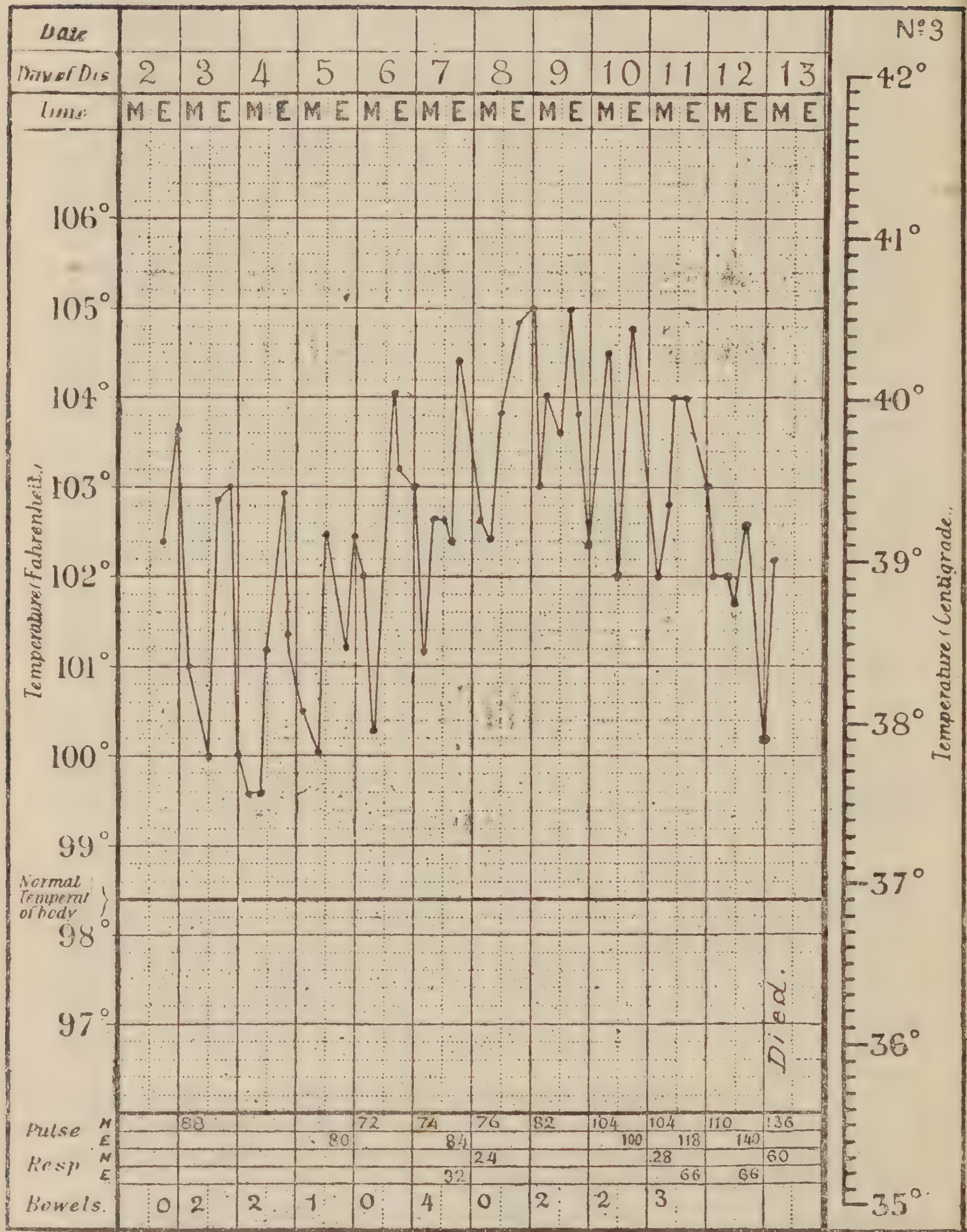
It is well to remember that when typhoid attacks a patient with malaria, the enteric onset may be very sharp and sudden and be associated with rigor. The temperature, however, soon becomes continuous. Often the curve fails to follow the typical course of typhoid so well known to the medical student.

The rise is usually abrupt even in non-malarial cases and is generally followed by a "high continued fever" which keeps steadily above 101° F. and for a long time does not vary more than 2° F. Towards the end of the third week it may swing a little and then descend by lysis. Another and severe type is the "continuo-remittent" where the temperature keeps up but shows a greater amplitude, producing a more spiked tracing on the chart (Fig. 76). Yet another remittent form closely simulates sub-tertian malaria (*see* p. 155).

Short abortive attacks are met with where the fever lasts only a few days. These may readily be missed in the absence of routine systematic blood cultures and agglutination tests, and missed, too, in spite of these aids to diagnosis.

In non-European races, whether African, Arab, or Indian, the disease conforms closely to the type met with in Europeans. Perhaps the slow pulse is its most characteristic feature. The old idea that there was a hybrid disease "typho-malaria" has been exploded. The two diseases not infrequently occur at the same time in the same patient and may modify each other in various directions.

Fig. 76.



Severe Typhoid with High Remittent Pyrexia, terminating fatally on thirteenth day. Typhoid Bacilli cultivated from finger blood on tenth day.—Rogers, "Fevers in the Tropics."

The help of the laboratory is usually required for the diagnosis of such a mixed infection. A chronic form of enteric fever sometimes lasting as long as a year is now a recognized entity.

Those cases which show little variation in the range of temperature, which runs steadily along a line in the neighbourhood of 103° F. or 104° F., for day after day and even week after week showing little or no amplitude even in a four-hourly chart, are liable to be specially dangerous and have a tendency to a fatal termination.

Diagnosis.—The diagnosis of typhoid fever, especially in the British soldier in the East, is apt to be a complicated problem. This is largely due to the fact that, having been previously "protected" by T.A.B. inoculation, little reliance can be placed on the result of at any rate one Widal reaction. It must be remembered that cases of undoubted typhoid fever may show no significant rise in specific agglutinins throughout the illness.

The only certain test is the isolation of *B. typhosus* on culture, from the blood, which can usually be effected, if proper precautions be taken, during the first week or ten days of a moderate or severe attack of the typhoid group. Occasionally blood cultures remain positive for a considerably longer period, and are often positive during a relapse. After fifteen days or so of fever positive cultures are more likely to be obtained from the fæces or, less commonly, from the urine, and daily specimens of both fæces and urine should be sent to the laboratory for this purpose. It should be noted that the presence of *B. typhosus* in the stools or urine merely denotes the carrier state and constitutes no absolute proof that the fever from which the patient is suffering may not be due to some other cause. It is usually safe to assume, however, that if the condition clinically suggests typhoid fever, the presence of *B. typhosus* in any of the secretions or discharges clinches the diagnosis. Total and differential white blood counts are of the greatest value in the differential diagnosis of fevers in the East and should never be omitted.

The detection of the carrier state is said to be facilitated by Felix's Vi-agglutination test.

Differential Diagnosis.—As already stated, malaria is the disease most difficult to distinguish from typhoid in the tropics when resort is had to clinical examination alone. Both diseases may exhibit chills, continued fever, bronchitis, enlarged spleen, tenderness and gurgling in the right iliac fossa, tympanites, diarrhœa, delirium and the typhoid state. Herpes indicates malaria, rose spots enteric, but, as noted, these are often absent in tropical typhoid.

Other diseases to be distinguished are paratyphoid fever and infections due to organisms of the *coli* group, *B. fæcalis alkaligenes*, etc., infective hepatitis, leptospirosis icterohæmorrhagica, influenza, especially the gastric form, bronchitis, rheumatism, cholecystitis and appendicitis. Also kala-azar, typhus fever, undulant fever, infective endocarditis, acute miliary tuberculosis, tuberculous meningitis, tuberculous peritonitis, a typhoid form of malignant hypertoxic syphilis described by French authors and pyæmic and septicæmic conditions. The French state that the pleomorphic bowel saprophyte called Thiercelin's enterococcus may sometimes produce a condition rather closely resembling enteric fever. Many

cases of infection attributed to the enterococcus were seen on the Gallipoli Peninsula and in Mudros, but little attention has been paid to this organism by British observers.

Prophylaxis.—Typhoid and paratyphoid fevers are spread by anything contaminated by the urine or fæces of patients and carriers so that the strictest attention must be paid to cleanliness and the rapid disinfection of all excreta, and all utensils, bedding, clothing, and other articles soiled by patients or their excreta. The organisms are frequently conveyed by the hands which therefore should always be washed before meals or before handling food or water, special attention being paid to the finger nails.

All water should be regarded as suspect and should be purified before being used for drinking or cooking ; this precaution should also be extended to aerated waters, and the sale of aerated waters and other drinks from unauthorized sources should be forbidden.

Food must be protected from flies, dust, and contaminated water, and special precautions should be taken against the adulteration of milk with polluted water. In the tropics all milk should be boiled or pasteurized under rigid supervision.

In hot countries, vegetables, especially lettuces, are a source of danger and should not be eaten uncooked, and only fruit which can be skinned, such as oranges or bananas, should be eaten raw. Oysters and other shell fish may be contaminated with sewage and should be avoided unless they come from beds known to be unpolluted.

The organisms can live in ice which should therefore not be put in drinks.

Cookhouse sanitation and the cleanliness of cooks must be of the highest standard, and no person who has suffered from any of the enteric group of fevers should be employed in the preparation or handling of food or on water duties. All persons so employed in tropical countries should undergo periodic laboratory examinations of their stools to ensure that they are not carriers.

Anti-fly measures should be carried out and special steps taken to prevent the access of flies to excreta and food. Conservancy measures must include the rapid and complete disposal of all excreta in such a way that water and food are not contaminated.

Inoculation is the outstanding prophylactic measure against the enteric group of fevers, especially in the case of young officers, soldiers, and their families proceeding abroad for the first time. Inoculation gives protection for one to two years, and to ensure the greatest measure of protection inoculations should be carried out at least three weeks before any special period of risk.

When typhoid fever is complicated by respiratory infection there is a distinct risk of droplet infection, and this must be guarded against.

Treatment.—Apart from the usual methods in vogue, mention may be made of the use of creosote as an antipyretic in cases where the reduction of temperature is desirable. Twenty to thirty drops are rubbed into the skin of the axillæ or flanks, and five drops floated on a diaphoretic mixture may also be given by the mouth. Compresses wrung out of alcohol, applied to the abdomen and covered with a cold water compress, may also be used for the same purpose. The water compress is changed every hour, that with

alcohol every two hours. If the skin is sensitive a little lanoline may be smeared on it. Where it can be managed cradling is useful combined with the use of ice. The heart requires special attention in the tropics.

Two drachms of Marmite daily may be given on general principles, and the administration of the juice of two lemons per diem, commenced when the temperature becomes normal, appears to lessen the liability to a complicating venous thrombosis.

Vaccine treatment is advocated by some in suitable cases, but this treatment must be commenced early if good results are to be expected. Less favourable results are obtained if the treatment is not commenced earlier than about the tenth day of the disease. Such cases may show no benefit at all. The usual initial dose is from 25 to 50 million, and a stock vaccine may be employed at first to save time, and replaced later by an autogenous vaccine if desired. The subcutaneous route is usually chosen for the injection, but some prefer intravenous administration.

Good results have been reported with *small* daily doses of sulphapyridine, *e.g.* 1·0 g. t.d.s., in conjunction with Felix's Vi-serum (one dose of 30 c.cm.).

Only small doses of the sulphonamide preparation are recommended in view of the danger that the leucopenia, which is normally present in the typhoid group of fevers, may develop into agranulocytosis in the event of any idiosyncracy to the drug on the part of the patient.

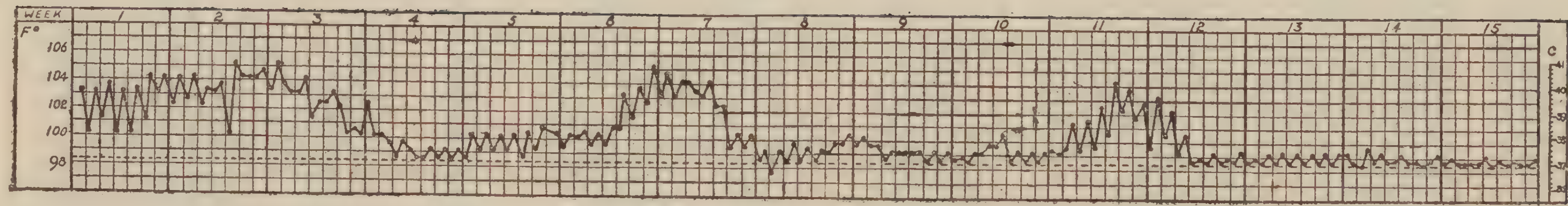
As in the case of the paratyphoid fevers (*see* page 181), a considerably more generous and varied diet is allowed by most authorities after the first few days of fever than was formerly considered advisable or safe. Rolleston recommends, after the first twenty-four hours, such readily digestible dishes as eggs, junket, mashed potatoes, apple sauce, chocolate, etc. In increasing the diet he considers that the physician should be guided by the appearance of the tongue, the character of the stools, and the condition of the abdomen; the last a very important consideration, as intractable flatulent distention is often a precursor of perforation.

UNDULANT FEVER

This long-continued fever is commonly known as Malta Fever, and has also been termed Mediterranean Fever and Gastric Remittent Fever amongst other titles. It has a wide geographical distribution throughout the Mediterranean littoral and is known to occur in Nigeria, Uganda and Southern Africa, as well as in India, China, Hong Kong, the West Indies, etc. The distribution is probably even more extensive than is realized at present, for the disease is readily confused with others if the possibility of its occurrence is not borne in mind, and the disease may now be regarded as cosmopolitan.

During the past few years undulant fever due to the organism of contagious abortion has been found to be widespread in Europe, America, and elsewhere.

Fig. 77



Temperature Chart from Typical Case of Undulant Fever covering fifteen weeks.

Etiology.—The cause of the classical form of undulant fever is *Brucella melitensis*. These minute cocci or cocco-bacilli are found in the blood and give rise to an acute or chronic septicæmia. Goats are apt to harbour the organism and excrete it in their milk, so much so that the drinking of goats' milk is the principal method of acquiring the disease. As in typhoid, food, fingers and flies are all probably operative in spreading infection, for, apart from milk, its products, such as cream and cheese, may harbour the organism; surface soil and dust may become contaminated from the urine of human beings, goats and other ruminants suffering from the disease and so lead to food infection; carrier cases doubtless play a part; and flies may acquire the micrococcus from the urine or fæces. Infection can take place through the skin and mucous membranes. The urine of ambulant human cases is, in all probability, a special source of danger. At the same time these additional methods of conveyance of the virus cannot bulk very largely or there would certainly have been many more cases during the last war.

Brucella abortus and *B. suis*, the causative organisms of contagious abortion of cows and pigs, may give rise to undulant fever in man. Such infections cannot be differentiated clinically though, on the whole, the organism of contagious abortion gives rise to a milder attack.

Symptoms.—Incubation period of six days to three weeks, usually fifteen days, followed by headache, insomnia, malaise, and anorexia. Constipation is the rule, and there is early splenomegaly and tenderness over the spleen. The temperature, of a remittent type, gradually rises, strongly suggesting the onset of typhoid. There may be epistaxis, and slight bronchitis and cough with profuse sweats are not infrequent. The tongue is flabby and coated with a silvery fur, the tip and edges remaining clean. Even at this stage joint troubles and neuralgia may put in an appearance, but they are usually deferred till a later period. After rising for three or four days by a step-like ascent the temperature falls by a similar descent and reaches normal on or about the tenth day.

The symptoms abate, the patient feels better for a few days, but the night sweats and the emaciation, which sets in early, continue and then the first of a long series of relapses manifests itself (*see* Fig. 77).

During these relapses the joint troubles arise, one joint usually being involved. There is no redness, but the part is swollen and there is effusion with severe pain. The condition is transient, lasting a few days but too often reappearing in another articulation. The order of frequency, according to Hughes, is the hip, knee, shoulder, ankle, wrist, fingers, toes, elbow, intervertebral joints.

At the same time neuralgic pains set in, the peripheral nerves being specially affected and the sciatic often involved.

Albuminuria may be present and orchitis occasionally occurs as a late symptom. One testicle, only, is normally involved and complete recovery is the rule.

The febrile waves follow each other at short intervals and the disease runs its wearisome average course of sixty to seventy days, which may, however, extend to wellnigh a year. Naturally the

patient becomes anæmic, he suffers from palpitation, his pulse is rapid and irregular. Mental depression lays hold of him, and it is important to remember that he may become a victim of the morphia habit. The total white count may be within normal limits or, more often, there is a moderate leucopenia (4,000 W.B.Cs. per c.mm.) with a relative lymphocytosis.

While this is the usual undulatory fever the disease may be ambulant in type, or there may be an intermittent form running a mild course, or the attack may be malignant with a high continued fever, pulmonary complications and a tendency to hyperpyrexia. The undulating type of fever is the most common, the febrile waves varying from ten days to six weeks. Intermissions of normal temperature usually last from seven to twelve days, but may be as long as a month. The temperature usually climbs and falls by step-ladder gradations, but the rise and fall may be abrupt.

When the undulating character is present the recurring waves usually become progressively shorter with increasing intermissions.

The severity of the disease cannot be gauged by a perusal of the temperature chart alone. The duration of the pyrexia is usually two to three months, but may vary within wide limits, up to two years.

The intermittent form is apt to be puzzling, as the morning temperature may be normal or sub-normal and the evening rise slight. Except in the malignant form the ultimate prognosis as regards life is good, only about 2 or 3 per cent. of the cases ending fatally.

Complications.—Arthritis, phlebitis, orchitis, neuralgia and hæmorrhagic manifestations may be mentioned. Pulmonary complications are also not uncommon and gastric and intestinal ulceration may occur.

Diagnosis.—This is best established by blood culture. The causal organism has been isolated from the blood of a chronic case one year after the onset. Agglutination tests are also of value provided they are properly controlled. An intradermal test, the meliten test, has been recently introduced. This consists in the intradermal injection of 0·2 c.cm. of a killed suspension of *Br. melitensis*: a positive reaction shows a red œdematous area at the site of inoculation. This test is less reliable than the agglutination reaction. The organism is excreted in the urine, and is generally present in large numbers at some time during the period of defervescence.

As already stated, the classical form of undulant fever is indistinguishable clinically from that due to the organism of contagious abortion. For isolation of the bovine strain of the latter, growth in an atmosphere of 10 per cent. CO_2 is necessary, whereas the swine strain will grow readily without this addition.

Differential Diagnosis.—Save where laboratory facilities are available, it is not always easy to diagnose undulant fever. It is apt to be mistaken for typhoid, paratyphoid, sub-tertian malaria, influenza, hepatic abscess, tuberculosis, especially phthisis, and, in certain regions, kala-azar.

The history and careful clinical observation will usually help to

clear up the case, but in no disease is bacteriological investigation more important.

Prophylaxis.—As for typhoid, special attention being paid to the disinfection of the urine. Isolation of human carriers, if they can be found. Boiling goats' milk, use of tinned milk, the slaying of infected goats and the avoidance of local products of milk.

Personal cleanliness as a preventative is important.

Treatment.—No drug has any specific action on the disease. Yeast may be given in 2 drachm doses twice daily in the hope of increasing the polymorphs and reducing the tendency to neuritis. Marmite in drachm doses twice daily appears to be of benefit in this respect.

Aspirin and phenacetin are not over-safe considering the cardiac weakness. Morphia may be necessary, but the risk of the morphia habit being acquired in this disease should be remembered. The insomnia has to be combated by the usual hypnotics, and cardiac tonics are often indicated. Cold sponging and local anodynes for joint and nerve pains are useful. Depressing drugs such as quinine and the salicylates are harmful. The ter-valent antimonial preparation, Fouadin, has given good results in some hands. Striking results in some cases have been claimed with drugs of the sulphonamide group ; in others they have not been so successful.

500 c.cm. of blood transferred from a convalescent patient has been favourably reported on. Protein shock therapy (intravenous T.A.B., etc.) has also given good results.

Though a serum has been tried with some success, vaccine therapy is probably the most promising line of treatment, especially in sub-acute and chronic infections. Opinions vary as to the optimum commencing dose, which naturally depends mainly on the case itself. Using an ordinary vaccine, 50 million is a safe dose to begin with, and it can be repeated, or increased, in a few days according to the patient's reaction. The dosage is gradually worked up to several hundred millions if well borne. Some prefer to commence with a dose of about 10 million and give the injections more frequently. It is said that sensitized vaccines act best.

YELLOW FEVER

West Africa appears to have been the original home of yellow fever, whence slave ships imported the disease to the Americas. Here the first identifiable epidemic broke out in Barbados in 1647. It established itself in endemic foci in the Southern United States, Mexico, Central America, along the coast of tropical South America, and in the West Indies. From these localities widespread epidemics originated, involving southern Europe on many occasions, and at least one outbreak occurred in the British Isles, namely in Swansea in 1865, due to infection imported from Cuba by the ship *Hecla*. Although the range of yellow fever is much restricted to-day, endemic foci still persist in several States of Central and South

America, and also in British and Dutch Guiana. In Africa the endemic zone runs from the West Coast of Africa, just north of Cape Verde, along the southern border of the Sahara to the Anglo-Egyptian Sudan, thence bending southwards it passes through the southern two-thirds of the Nuba Mountains in Kordofan, across the White Nile, south of Jebelem, to the Sudan–Abyssinian border and probably into Abyssinia up to the edge of the plateau. The eastern border of the zone passes southwards through the western part of Uganda, immediately to the west of Lake Victoria, and thence diagonally south-west to the mouth of the Congo River.

Etiology.—Yellow fever is due to a virus which is present in considerable concentration in the human blood stream during the latter part of the incubation period and during the first three days of fever. Usually the blood is not infective after the end of the third day since the virus is then neutralized by immune bodies. Aragão, in his researches in Brazil, injected susceptible monkeys with the blood of sixteen patients after seventy-two hours' illness. He obtained only four positive results.

The virus when present in the blood is filterable through Berkefeld V and N filters ; its size, accurately estimated by passing through graded collodion membranes is from 18 to 27 mμ.

After an infective feed an *Aedes ægypti* mosquito is not capable of transmitting infection by bite for some days, the period varying in relation to the temperature. It may be as short as eight, as long as fifteen or more days, the average being about twelve days. The insect is then infective for the rest of its life, on an average about two months : *Aedes ægypti* cannot transmit the virus to its offspring, while contact infection from one mosquito to another does not occur.

The only proven vector of the disease in Africa is *Aedes ægypti* (=*Stegomyia fasciata*), a house-haunting species spread widely, but in the New World intermittently, between the latitudes of 40° N. and 40° S. (Fig. 14). It is most active in the afternoon and in the early morning, but if hungry may bite at any hour. A number of other African species of mosquito have been found capable of transmitting yellow fever by bite under laboratory conditions, but their rôle in nature is at present unknown. These experimental carriers are : *Aedes* (*Aedimorphus*) *stokesi*, *Aedes* (*Stegomyia*) *africanus*, *A.* (*S.*) *luteocephalus*, *A.* (*S.*) *simpsoni*, *A.* (*S.*) *vittatus*, *Eretmopodites chrysogaster*, *Tæniorhynchus* (*Mansonioides*) *africanus* and *Culex thalassius*. Among mosquitoes universally distributed in the tropics and capable of acting as vectors under laboratory conditions is *Culex fatigans*, while *Aedes albopictus*, found in India and the Far East, can also transmit the virus by bite. The means by which infection is maintained in endemic foci is still uncertain. There is, however, considerable evidence to show that the virus may persist in the absence of human infections. In the endemic zone in Africa and in South America about 20 per cent. of wild monkeys are found to have immune bodies to yellow fever. African monkeys are not insusceptible to yellow fever but the disease in them is inapparent, although the virus may circulate in the peripheral blood stream for a few days. There is some evidence that both wild and domestic

animals may become infected under natural conditions: in fact it is now generally believed that yellow fever is primarily a disease of animals which only on occasions attacks man. The introduction of a sufficient number of susceptible persons, however, provides the necessary combustible material for an epidemic.

Jungle Yellow Fever.—Recently it has been proved that yellow fever occurs in many forest districts in South America where *Aedes ægypti*, which is primarily an old-world species, has never penetrated. Jungle yellow fever has been described more especially in Brazil and Colombia. It must be distinguished from rural yellow fever, the only known vector of which is, as in urban epidemics, *Aedes ægypti*. In South American jungle yellow fever, although the virus is identical with that causing urban outbreaks, the proven vectors are *A. leucocelænus*, *Hæmagogus capricorni* and certain Sabethine mosquitoes; there is at present no evidence that true jungle yellow fever occurs in Africa where *Aedes ægypti* is very widely distributed under rural conditions.

Symptoms.—The incubation period is usually from forty-eight hours to just over six days, but may extend to as long as ten days. Occasionally prodromal symptoms, malaise, headache and giddiness, are in evidence for a day or two, but the onset is usually abrupt, sometimes with a feeling of chilliness which may amount to a rigor. There are marked frontal headache, perhaps so intense as to make the patient cry out, and racking pains in the back and limbs. As the temperature rises, the face, at first pale, becomes red and turgid, and the eyes bright and watery, with fine injection of the conjunctivæ. The eyelids are swollen and drooping. The appearance of the patient may suggest scarlet fever, an error which in one instance was directly responsible for almost 150 deaths. During this time the temperature rises and reaches its maximum, usually after about twenty-four hours, or a little longer. Temperatures over 104° F. are very rare in yellow fever. As a general rule those whose temperature does not rise above 103° F. recover. As a rule the pulse is rapid, but even at this early stage it may be slow in relation to the temperature. The muscular pains increase in severity and the patient may feel as if he had received a knockout blow—the "*coup de barre*" of old writers. The appetite is lost, the skin hot and dry, the tongue small, pointed, furred but with clean edges, and constipation is the rule. The patient is sleepless, restless and anxious. There is marked epigastric discomfort and tenderness, and vomiting of mucus, bile-stained fluid, or pure gastric juice commences ("white vomit"). The urine is diminished, and albumin, *in increasing amount*, appears usually on the second or third day.

The foregoing symptom-group constitutes the First Stage.

The Second Stage, that of remission, commences usually between the third and fifth days, and is characterized by a fall in the temperature and abatement of the symptoms. The redness and turgidity of the face disappear, and the conjunctivæ lose their suffusion but generally become icteroid. The attack may end here, but usually after a lull of from a few hours to a day or two, vomiting recommences, the temperature rises, and the patient enters on the Third Stage.

The outstanding features of the Third Stage are black vomit, melæna, and jaundice. The vomit varies from a clear liquid containing dark flakes, to a thick uniform black fluid. Jaundice of any shade of yellow may be observed, sometimes of marked intensity. It is apparent first in the conjunctivæ (usually during the stage of remission) and spreads to the face, neck and chest. Generalized jaundice is seen only when the disease is prolonged, that is to say, most frequently in cases of recovery. The urine diminishes in quantity and the albuminuria continues to increase. There is often a marked dissociation of the temperature and the pulse rate. With a constant temperature there is a falling pulse rate, with a rising temperature the pulse rate is constant. In addition to the black vomit, other hæmorrhagic signs are common—melæna, purpuric spots, bleeding of the gums, lips, tongue, bladder, vagina—and vision may be destroyed by extravasation of blood into the eye. Toxæmia increases, hiccup sets in, and the patient dies in a state of exhaustion, coma, or convulsions.

In more favourable cases, improvement may set in during the third stage, the unfavourable symptoms ameliorate, and convalescence is rapidly established. According to the degree of severity of yellow fever, three clinical grades have been described :—

Mild.—Even in Europeans the attack may be so mild as to be mistaken for influenza. Slight headache and backache with fever lasting for forty-eight hours may constitute the only symptoms. Albuminuria may be entirely absent or very transitory.

Severe.—The appearance in the stage of remission of the characteristic symptoms—jaundice, vomiting, hæmorrhages, anuria, mental disturbance, slow pulse.

Grave.—The symptoms just detailed appear during the first stage. Marked involvement of the nervous system. The attack may assume a " pernicious " type, with apoplectic, choleraic, or algid symptoms. In the last named there may be no jaundice.

Morbid anatomy.—The only specific changes are found in the liver. In patients dying in the acute stage the following microscopical changes are found : A jumbling of the trabeculæ, as if the liver cells had been thoroughly shaken, more accentuated in the mid-zone of the lobule than elsewhere ; fatty degeneration of varying intensity generally more abundant in the central and peripheral than in the mid-zone of the lobule ; an absence of complete necrosis of the central zone of the liver lobule ; a few non-necrotic cells can always be found among the cells immediately adjacent to the central veins even when at first sight all the cells seem to have undergone an acidophilic change ; what has been called a " salt and pepper " distribution throughout the entire lobule with greatest prevalence in the mid-zone of rounded refractile acidophilic bodies, the so-called Councilman bodies. These acidophilic bodies sometimes show the " shadows " of nuclei within them ; they are the remains of parenchymatous cells that have undergone a specific type of necrosis. Other changes in acute cases are a varying degree of leucocytic infiltration, principally of mononuclear cells, most pronounced in the mid-zone ; yellow pigment inside the parenchymatous cells of the central zone ; hyperæmia of the sinusoids,

especially in the mid-zone; nuclear changes. The nuclear changes consist of œdema and intranuclear inclusions; the latter consist of acidophilic material and are associated with margination of the basophilic chromatin on the nuclear membrane. Intranuclear inclusions are not well preserved by material fixed in formol or formol saline, and Zenker's fluid, without acetic acid, should be used whenever possible; portions of liver to be fixed should not exceed 1 c.cm. Intranuclear inclusions are only seen in about 20 to 30 per cent. of human liver cells, except in some epidemics, as in Accra in 1937, when 70 to 80 per cent. of the liver cells exhibited this change.

In patients who have died after the eighth day of illness there may be only a few Councilman bodies, but their place is taken by masses of bright ochre-coloured granules lying either free among the non-necrotic parenchymatous cells or more often within macrophages and Kupffer cells. These ochre-coloured bodies are the last stages of degeneration of the hyaline Councilman bodies, probably impregnated with bile pigments.

Diagnosis.—It should be emphasized that there is no one clinical feature which is characteristic of yellow fever. Exact diagnosis of yellow fever can only be made by one of the three following methods:

(1) Isolation of the virus from the blood during the first three days of fever.

(2) Histological examination of the liver in fatal cases.

(3) A mouse-protection test for immunity, blood being taken during the first few days of illness and again during convalescence.

(1) Isolation of the virus can only be carried out as long as the virus is present, free in the blood, unneutralized by antibodies.

The following animals are susceptible: the Indian rhesus monkey, *Macaca mulatta*, hedgehogs, both the European and various African hedgehogs, and the mouse.

Monkeys and hedgehogs should be injected with 1 c.cm. of blood intraperitoneally; monkeys should have their temperatures taken daily, a temperature of 104° F. or over is significant. The disease in monkeys usually takes about three days to develop and death may occur from three to four days later. Hedgehogs die in from seven to twelve days; both in rhesus monkeys and hedgehogs the lesions are similar to those found in man. Some strains of the yellow fever virus, however, cause neither fever nor death in rhesus monkeys; if these animals are inoculated blood should therefore be removed from the heart on the fifth day after inoculation and serum injected into mice. When mice are inoculated with yellow fever blood, they should be injected intracerebrally with 0·03 c.cm. of serum, the point of inoculation being over the vertex of the skull and just to one side of the middle line. If newly-born mice are available they can be inoculated intraperitoneally. Symptoms of encephalitis begin to develop in from nine to twelve days; death taking place two to three days later.

In removing blood from patients with suspected yellow fever, it is important that rubber gloves should be worn unless the operator

has himself been immunized. If the blood is to be forwarded to a laboratory it should be placed in a thermos flask and packed with ice and salt.

(2) Portions of liver can be removed without carrying out a full post mortem by means of an instrument known as a viscerotome. Viscerotomes are now widely used in South America and are available in Africa. Many Africans, both Mohammedans and pagans, object very strongly to mutilation of the corpse after death.

Extensive burns may give rise to liver changes not unlike those seen in yellow fever.

(3) The mouse-protection test. This test, which is highly specific for immune bodies to yellow fever, consists in the injection of mice with a neurotropic strain of the yellow fever virus and the serum to be tested. If the serum contains immune bodies the mice survive. By using dilutions of serum the test can be rendered quantitative. A single positive mouse-protection test signifies that the patient has at some time or another become immunized against yellow fever. A negative test at the beginning of an illness and a positive test during convalescence show that the illness must have been due to yellow fever. At least 15 c.cm. of blood should be removed for a mouse protection test. The blood should be allowed to clot and no preservative should be added.

Differential Diagnosis.—Leptospiral jaundice : Leptospira can be isolated from the blood and urine, and the infection is easily transmitted by inoculating the scarified skin of the guinea-pig. In leptospiral jaundice there is almost always a polymorphonuclear leucocytosis, in yellow fever almost always a polymorphonuclear leucopenia. Malaria, blackwater fever, relapsing fever and any short fever with jaundice, have to be distinguished. Infective hepatitis is common throughout Africa; occasional patients may develop jaundice and black vomit, dying with acute or sub-acute liver necrosis. Dengue, also transmitted by *Aedes ægypti* and therefore to be met with in the same districts as yellow fever, bears a strong resemblance to a mild attack of the latter disease. In the Greek epidemic of dengue some severe cases had jaundice and black vomit. Durand's disease, a virus infection described in Tunis, may also cause black vomit ; while Rift Valley fever, Bwamba forest virus and West Nile virus may simulate a mild attack. It should be remembered that many Africans develop jaundice with lobar pneumonia, while sickle-celled anæmia may also cause acute attacks of jaundice.

Treatment.—Every drug likely to be helpful has been tried in yellow fever, but none yet discovered has any curative effect. Rest the stomach as far as possible, avoiding milk, and give iced water, iced sugar water, or alkaline drinks, in the hope of preventing mechanical blocking of the kidneys. An ice-bag applied to the epigastrium is sometimes of marked benefit in relieving distress. Intravenous injections of 5 per cent. glucose, half a pint at a time, have much to commend them if glucose cannot be taken by the mouth. When large quantities of glucose are being taken five to ten units of insulin daily are of value. The serum of convalescents

or hyperimmune serum, if given during the incubation period may abort or at any rate reduce the severity of the attack. Such sera are, however, quite valueless in treatment once symptoms have been observed.

Prophylaxis.—There are three essentials in the prophylaxis of yellow fever :—

(1) Early diagnosis of cases.

(2) Immunization.

(3) Eradication of mosquitoes.

Early Diagnosis.—The methods necessary for *exact diagnosis* have already been described. If the first case or cases escape undiagnosed a second crop will appear in about a fortnight's time and an epidemic may rapidly assume gigantic proportions. In the Sudan outbreak of 1941 at a conservative estimate there were 30,000 cases.

Immunization.—Immunization is carried out by means of a single inoculation of yellow fever virus vaccine. The vaccine is prepared by cultivating an attenuated strain of the yellow fever virus on the chorio-allantois of the developing chick embryo. The tissue culture virus is dried by the low-temperature-reduced-pressure method and maintained in sealed ampoules. The virus is, however, still living and is relatively unstable. The vaccine will only retain its full potency if it is stored continuously at a temperature that is not raised above 0° C. During transportation special precautions are needed to ensure that a low temperature storage is maintained.

Unless the vaccine is active, immunity will not develop in the inoculated individual. When, therefore, it is necessary to store the vaccine for any prolonged period animal inoculation tests should be undertaken from time to time to ensure potency before use.

For administration, the vaccine is reconstituted by the addition of cold sterile distilled water. It is important to see that the sterilized syringe and needle are cool before the vaccine is taken up and also that any of the vaccine not used within an hour of reconstitution should be discarded.

Very large numbers of individuals have now been immunized in South America and West Africa, and also in this country before they proceed to West Africa. As a rule there is little or no reaction ; only a very small proportion develop a slight headache and malaise some five days after the injection. Immunity develops about ten days after the inoculation and lasts for at least two years. The Interdepartmental Committee on the Control of Yellow Fever, set up by the Secretary of State for the Colonies, has not only recommended large-scale immunization within the endemic zones in Africa, but has also recommended that all travellers passing through an actual endemic zone to a potentially endemic area should also be immunized. The endemic zone in Africa may be considered as lying between 14° N. on the one hand and the southern boundaries of the Belgian Congo and Tanganyika Territory on the other hand.

Mosquito Destruction.—Known or suspected cases of yellow fever should be isolated in screened quarters or kept under mosquito nets night and day. All mosquitoes in infected houses must be

hunted down and destroyed by fumigation, spraying and swatting. All houses within a radius of at least 40 yards, and preferably more, of an infected house should be dealt with in this way. Everyone in the neighbourhood should use mosquito nets with great care unless their habitations are effectively screened.

Aedes ægypti is essentially domestic in its habits and breeds in and around houses in tanks, sagging gutters, tins, domestic utensils, flower vases, and every kind of vessel or container which holds water. This mosquito also breeds in tree holes, for example in baobab trees, *Adansonia digitata*, at considerable distances from houses. If holes are numerous the trees should be felled ; if there are only a few holes they should first be creosoted and the interiors then filled with earth and coalas or other liquid tar preparation. This does not crack in the way that cement does.

An intensive and tireless campaign must be waged against the vector in all its stages ; fortunately it is the easiest of all mosquitoes to eliminate. It should be remembered that eggs withstand drying for prolonged periods and may hatch out months after being laid if they come in contact with water.

Quarantine.—In order to prevent the spread of yellow fever from endemic areas to those in which yellow fever does not exist, but where there may be conditions which permit its development, travellers passing through such zones are subject to certain quarantine regulations. At the present time these regulations vary according to the Government or Administration responsible for the territory in question. The Interdepartmental Committee on Yellow Fever Control has recently, in its First Interim Report, put forward concrete recommendations for the unification of all such regulations as applied to the Western Hemisphere. If these are fully accepted their implementation will do much to simplify the administrative control of this disease.

APPENDIX

ZOOLOGICAL NOMENCLATURE

It is hoped that the following notes will be helpful to medical officers in writing reports which necessitate the employment of names of animal parasites.

The present system of binominal nomenclature was formally introduced for the animal kingdom in 1758 by the great Swedish naturalist Linné, usually known in this country under the latinized name, Linnæus. On the Linnæan system the present International Rules of Zoological Nomenclature are based.

These were adopted by an International Congress of Zoology, and later congresses appointed a permanent International Commission on Zoological Nomenclature which concerns itself with the various questions arising in connexion with the Code.

Before dealing with any of the actual rules, it might be well to give a simple explanation of the method of classification adopted for animals. Take as an example the common fly, *Musca domestica*. All individuals included within this conception resemble one another in every specific point, other than such differences as are due to sex and to slight individual variation. Under suitable conditions these flies will breed and produce fertile offspring. Consequently they are regarded as constituting a species, *M. domestica*. Out of doors in England we are often pestered by flies resembling *M. domestica* very closely, but whereas the male *M. domestica* has a fairly broad space between the eyes, this other fly has his eyes set close. This constant difference, *inter alia*, shows that we are dealing with another species, in this case *Musca autumnalis*. But these two species, together with many others, have in common the same wing venation, the same arrangement of certain bristles, etc., characteristics which are sufficiently distinct to be considered of generic importance. So all the species showing these are grouped together to form a genus, *Musca*. From this it is evident that the designation of a species consists of two parts, the name of the genus to which it belongs, combined with its own specific name. To proceed further, if the genus *Musca* is compared with the genus *Glossina* (tsetse flies), with *Stomoxys*, etc., these genera are found to have certain features in common, and so all which show these characters are grouped together in a family—MUSCIDÆ. By a similar method the MUSCIDÆ are combined with other related families to form an order—DIPTERA, and the DIPTERA are joined with other orders (fleas, bugs, lice, etc.) to form a class, INSECTA. The INSECTA, together with the ARACHNIDA (Ticks and Spiders) and certain other classes, constitute the Phylum, ARTHROPODA, other phyla of medical interest, built up by a similar grouping being the parasitic flat worms, parasitic round worms, molluscs, etc. And this pedigree carried back still further will ultimately join up with

that of the more lowly animals, the PROTOZOA, this final assemblage of METAZOA and PROTOZOA constituting the animal kingdom.

For convenience in classification, divisions intermediate between these may sometimes be recognized—suborders, subfamilies, subgenera, etc., and the individuals of a species, especially one which is large and widespread, may show small constant differences indicative of racial varieties or subspecies.

The individual specimen on which the original description of a species is based is known as the "type" of that species. The modern founder of a species deposits the type in some museum or collection where it is available for future reference. Unfortunately the types of many of the older species are now non-existent or unknown, a deprivation which may render the original verbal description difficult to interpret. Similarly a definite species is taken as the type of a genus, usually, though not necessarily so, the earliest named species in the genus. *Culex pipiens*, for example, is the genotype of *Culex*, and although this genus subsequently may be expanded or contracted, the generic characters of *Culex*, however regarded, must be such as to include the genotype, *C. pipiens*.

We may now consider the rules of nomenclature so far as they concern us.

Article 2.—" The scientific designation of animals is uninominal for subgenera and all higher groups, binominal for species, and trinominal for subspecies."

Thus, human head and body lice belong to the genus *Pediculus*, the species is *Pediculus humanus*, and if desired to go further and contrast the two subspecies a trinominal designation is necessary, *e.g. Pediculus humanus corporis*. (Article 17 directs that when a subspecific name is cited it is to be written directly after the specific name without the interposition of any mark of punctuation.)

Article 3.—" The scientific names of animals must be words which are either Latin or Latinized."

Various directions are given in the body of the Code and in the Appendix for Latinizing words of Greek and of barbaric origin. For instance, the Greek terminal *os* has to become *us*, so that the name of the well-known genus of ticks is correctly rendered *Ornithodorus*. There is no objection to the terminal Greek *a*, therefore it is unnecessary to Latinize the common *-stoma* to *-stomum*.

Article 4.—" The name of a family is formed by adding the ending *idæ*, the name of a subfamily by adding *inæ*, to the stem of the name of the type genus."

Thus from *Culex*, the type genus of the mosquito family, we have CULICIDÆ and CULICINÆ.

Article 8.—" A generic name must consist of a single word, simple or compound, written with an initial capital letter, and employed as a substantive in the nominative singular."

Article 10.—" When it is desired to cite the name of a subgenus, this name is to be placed in parenthesis between the generic and specific names."

Many authorities regard *Stegomyia* as a subgenus of *Aedes*, which would be expressed by the form, *Aedes* (*Stegomyia*).

Article 13.—" While specific substantive names derived from names of persons may be written with a capital initial letter, all other specific names are to be written with a small initial letter."

Article 19.—Under this article there is a Recommendation : " For scientific names it is advisable to use some other type than that used for the text." Usually the names of genera, and lower groups, are italicized, roman type being employed for those of higher divisions.

Article 22.—" If it is desired to cite the author's name, this should follow the scientific name without interposition of any mark of punctuation ; if other citations are desirable (date, etc.), these follow after the author's name, but are separated from it by a comma or by parenthesis."

Article 23.—" When a species is transferred to another than the original genus, or the specific name is combined with any other generic name than that with which it was originally published, the name of the author of the specific name is retained in the notation but placed in parenthesis. If it is desired to cite the author of the new combination, his name follows the parenthesis."

Pediculus humanus Linnæus, 1758, can be taken as an example under Article 22. Whereas (Article 23) *Phthirus pubis* (Linnæus, 1758) Leach, 1815, shows that Linnæus named this species, but placed it in a different genus (*Pediculus*), from which it was removed to its present genus by Leach.

Article 25.—" The valid name of a genus or species can be only that name under which it was first designated on the condition :—

" (*a*) That the name was published and accompanied by an indication, or a definition, or a description.

" (*b*) That the author has applied the principles of binary nomenclature."

This is the all-important Law of Priority.

Article 26.—" The tenth edition of Linné's ' Systema Naturæ', 1758, is the work which inaugurated the constant general application of the binary nomenclature in Zoology. The date, 1758, therefore, is accepted as the starting-point of Zoological nomenclature and of the Law of Priority."

Article 32.—" A generic or a specific name, once published, cannot be rejected, even by its author, because of inappropriateness."

The discovery that *Necator americanus* (Stiles) is widely distributed in the old world does not affect the validity of this name.

Article 34.—" A generic name is to be rejected as a homonym * when it has previously been used for some other genus of animals."

Owen, in 1835, founded a genus *Trichina* for the parasitic worm which causes trichinosis. This name was rejected, as it had been applied to a genus of insects by Meigen in 1830. Subsequently Owen's genus was named *Trichinella*.

---

* A homonym is one name for two or more things ; a synonym more than one name for the same thing.

Article 35.—" A specific name is to be rejected as a homonym when it has previously been used for some other species of the same genus."

It will be noted from the preceding two articles that a generic name once promulgated is preoccupied as regards the whole animal kingdom, whereas the specific name is preoccupied only within its own genus. Thus, there can be only one genus " *Pulex*," and only one species of *Pulex* named " *irritans*," but it would be permissible to have an *Anopheles irritans*, a *Culex irritans*, and so on for every genus of animals.

Medical men often complain bitterly of the " continual changing of names," but most of the trouble they experience in this respect has arisen from the retention of obsolete nomenclature in medical text-books and teaching centres. No person now alive, other than those given to archæological delvings, should ever have heard of " *Pediculus* " *pubis* or " *Acarus* " *scabiei*, for this terminology was discarded on the breaking up of these old composite genera over a hundred years ago. It must be admitted, however, that some austere systematists fail to remember that the Rules of Nomenclature were made for man, and not man for the Rules of Nomenclature. None the less, a wise adherence to the code is the only means of evolving order out of chaos. Eventually, when the dozens of superfluous names which have been showered on various animal parasites have been eliminated, the happy student will have to know only one name for each species. So long as the principles of nomenclature remain a mystery to us, names are necessarily employed in a haphazard and unreasoning fashion, for the reasons determining the selection of a term cannot be understood nor its form comprehended, and being blind ourselves we cannot discern if the guides whom we helplessly follow are themselves gifted with vision.

INDEX

A.

B.

C.

D.

H.

I.

J.

K.

L.

M.

N.

O.

P.

Q.

R.

T.

U.

V.

W.

X.

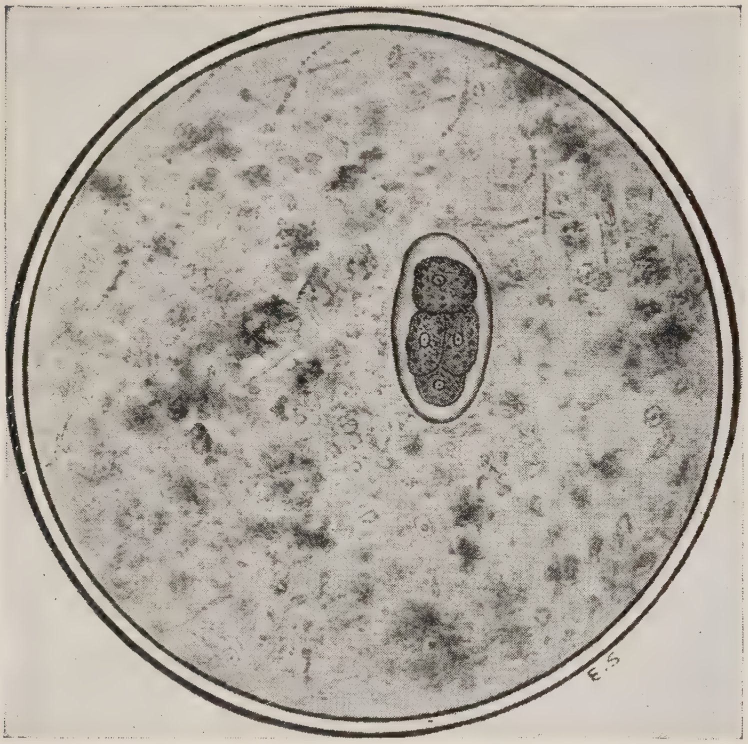
Y.

Z.

Printed under the Authority of HIS MAJESTY'S STATIONERY OFFICE
by William Clowes & Sons, Ltd., London and Beccles.

19/3/41 (2032) Wt. 669—8905. 10M. 5/43. W. C. & S., Ltd. Gp. 395.
S.O. Code No. 57-45-0-42*

Plate 1.



Microscopical preparation showing Ancylostome Egg in human fæces.
(Partly after Bass and Dock.) (Wellcome Bureau of Scientific Research.)

Plate 2.

Ornithodorus moubat

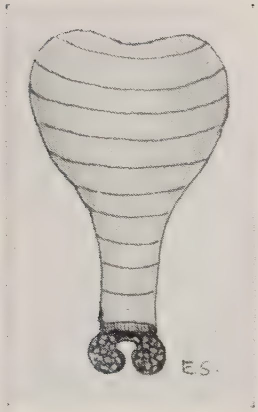
Plate 3.

Glossina morsitans. ×4. (After Graham.)

Plate 4.

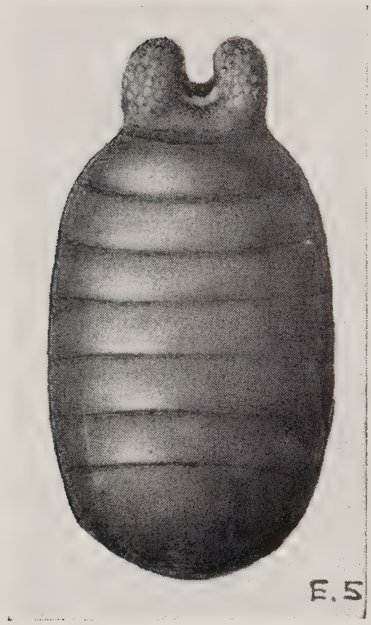
Glossina palpalis. ×4. Original by E. Schwarz.
(Wellcome Bureau of Scientific Research.)

Plate 5



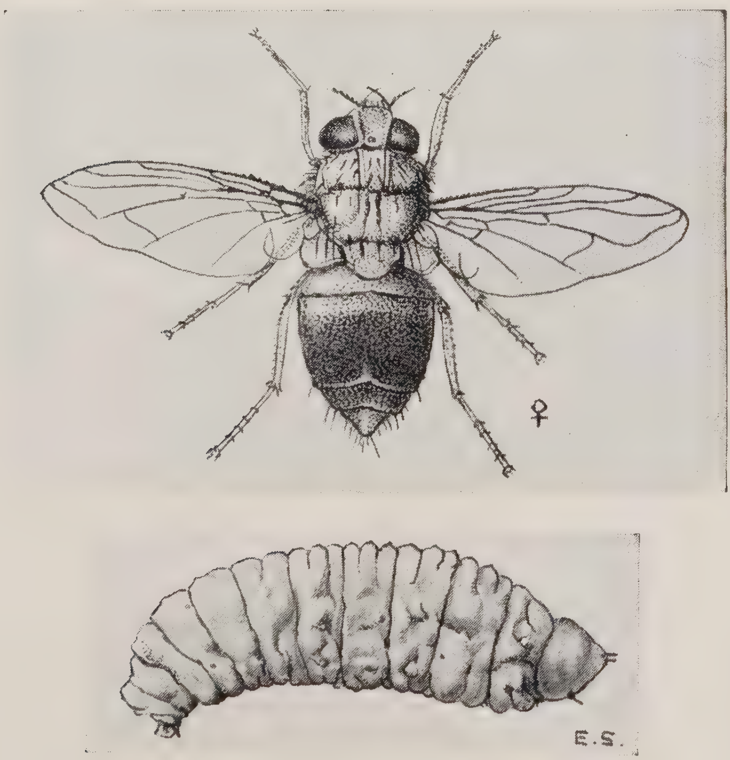
Larva, *Glossina palpalis*, Original size, 7–7½ mm. length. (After Rouband.)

Plate 6.



Pupa, *Glossina palpalis*. (After Graham.) Original size, 5½ mm.

Plate 7.



Auchmeromyia luteola and larva. (After Manson.)

Plate 8.

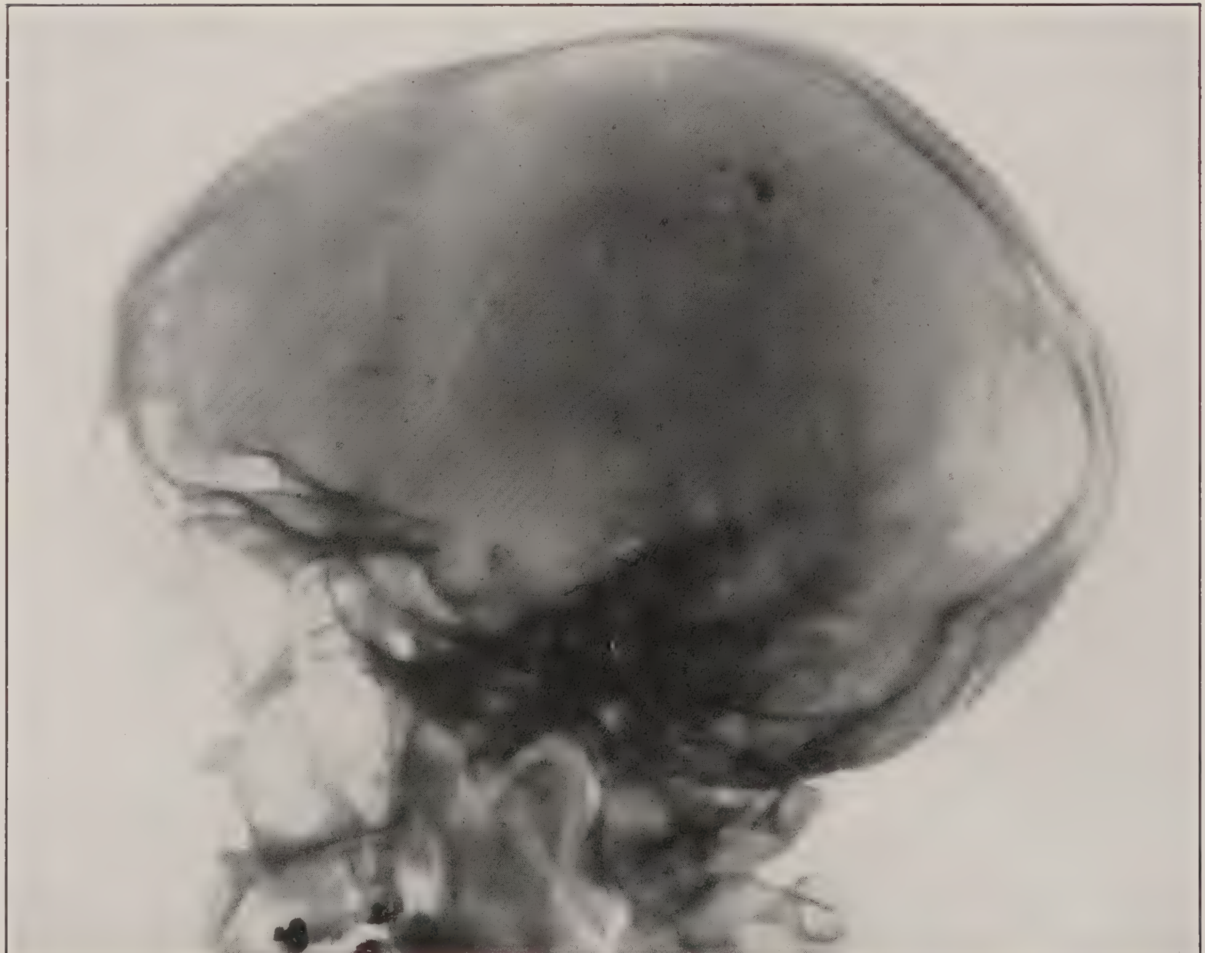
Cordylobia anthropophaga, the Tumbu Fly and its larva.
(Wellcome Bureau of Scientific Research.)

Plate 9.

Section of human brain containing an undegenerated and seemingly living larva of *T. solium*. Infestation of not less than fifteen years' duration. Note scolex with sucker and hooklets and collapsed bladder wall. The reactionary zone in the brain tissue is clearly seen.

(*British Encyclopedia of Medical Practice, Vol. III.*)

Plate 10.



Radiograph of skull showing one calcified cyst towards vertex and several calcified scolices scattered throughout the brain. Calcification in the brain, when it occurs, appears mainly to affect the scolex.

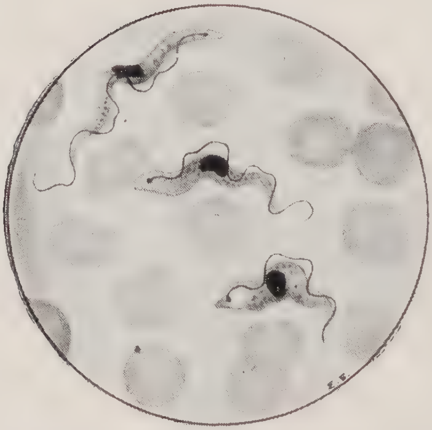
Plate 11.

Numerous oat-shaped cysts lying in the muscles of lower limb.

Plate 12.

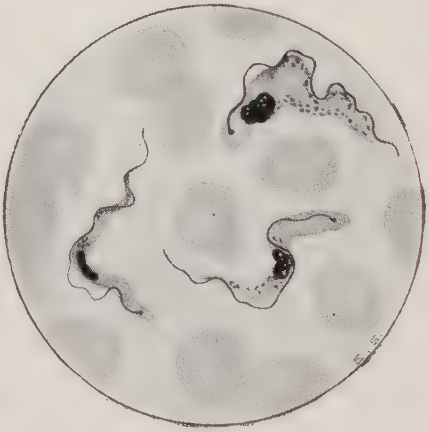
Heavy infestation of lower limb with cysts of approximately the same size and shape.

Plate 13.



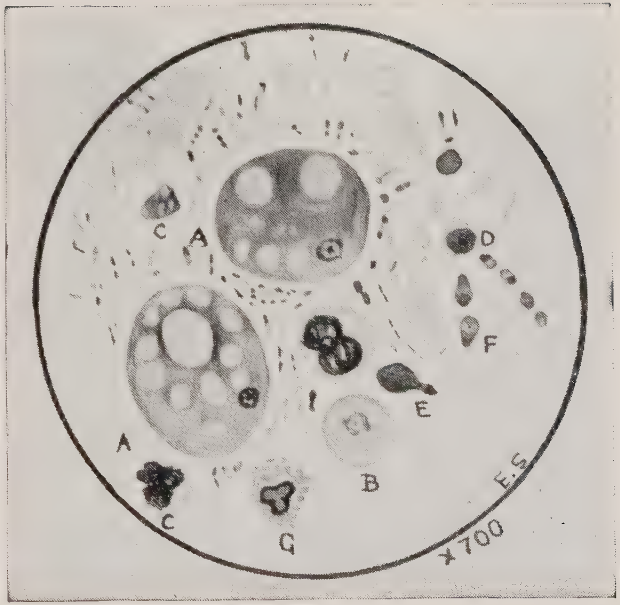
Trypanosoma gambiense, showing long, intermediate and stumpy forms. (Partly after Bruce.)

Plate 14.



Trypanosoma rhodesiense, showing long, intermediate and stumpy forms. (Partly after Bruce.)

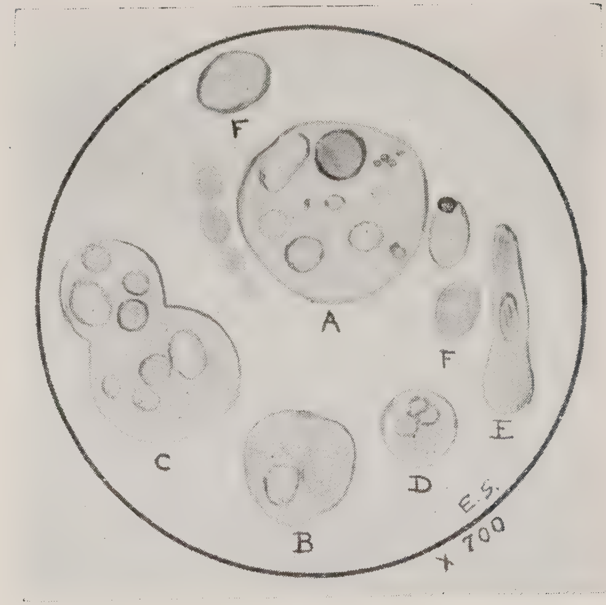
Plate 15.



Amœbic dysentery.

A—Ent. histolytica with ingested red cells.
B—"Minuta" form.
C—Nuclei of disintegrated polymorph leucocytes.
D—Nuclei of semi-digested leucocytes.
E—Yeast cell.
F—Clostridium butyricum.
G—Eosinophil cell.

Plate 16.



Cells in freshly passed bacillary dysentery stool.
Shiga bacillus.

A—Macrophage cell showing nucleus, ingested red cell, chromatoid bodies and fat globules.
B—"Refractile cell" with apparent nucleus.
C—Macrophage with daughter cell.
D—Polymorphonuclear leucocyte.
E—Columnar epithelial cell.
F—Red cell.

(After Manson-Bahr and Willmore.)

Plate 17.

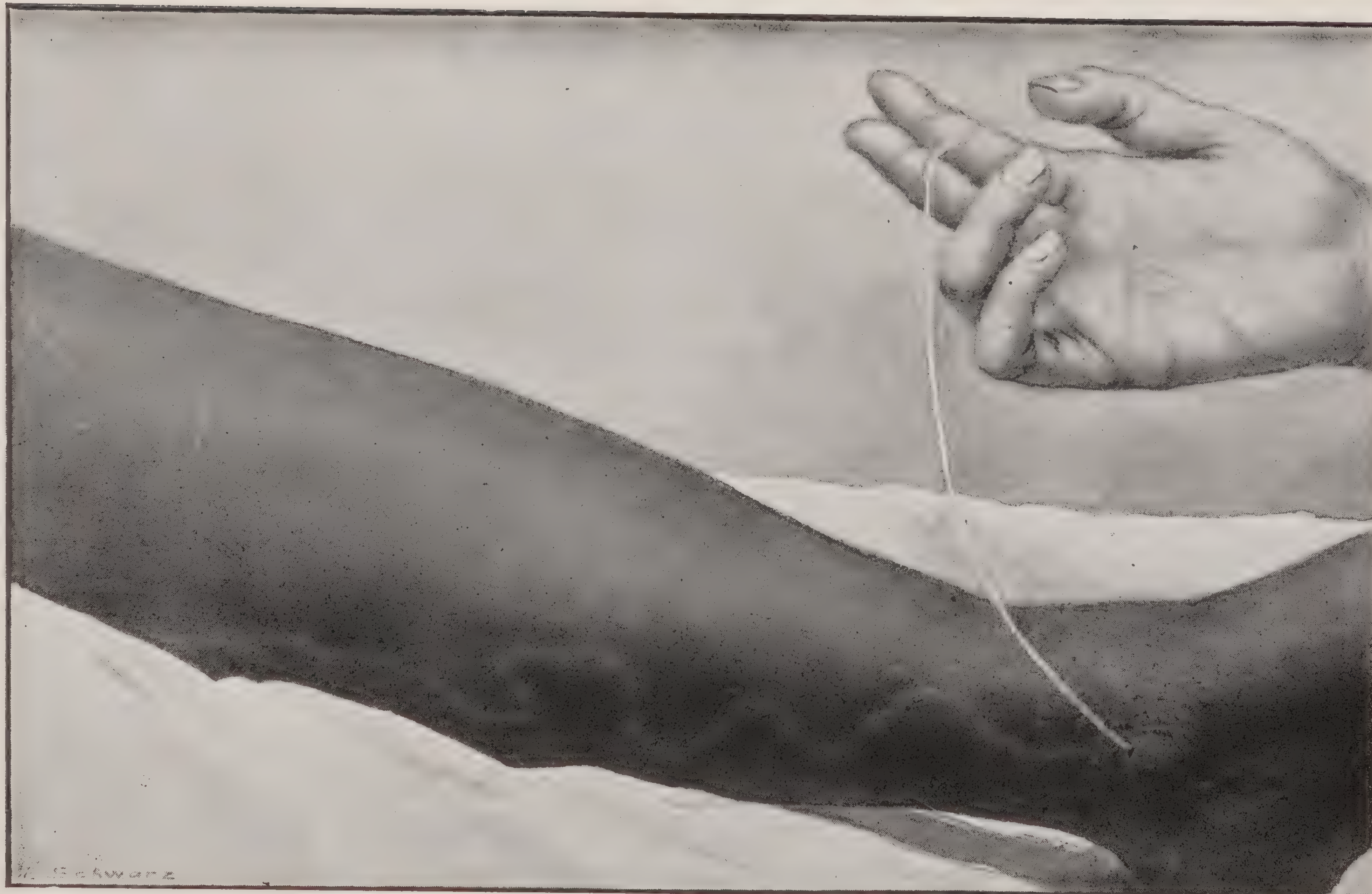
The extracorporeal development of the human coccidium, *Isospora hominis* (=*belli*), as it occurs after being passed in the fæces. On the ground or in the water the oöcyst becomes infective by development as shown in Figs. 1–4, producing finally within it two sporocysts each containing four sporozoites and a residual mass of protoplasm. The cysts of several species of *Eimeria*, another genus of coccidium, may be swallowed in infected fish and appear in the fæces. No *Eimeria* is known to parasitize man.

Plate 18.

Embryos of *D. medinensis*.

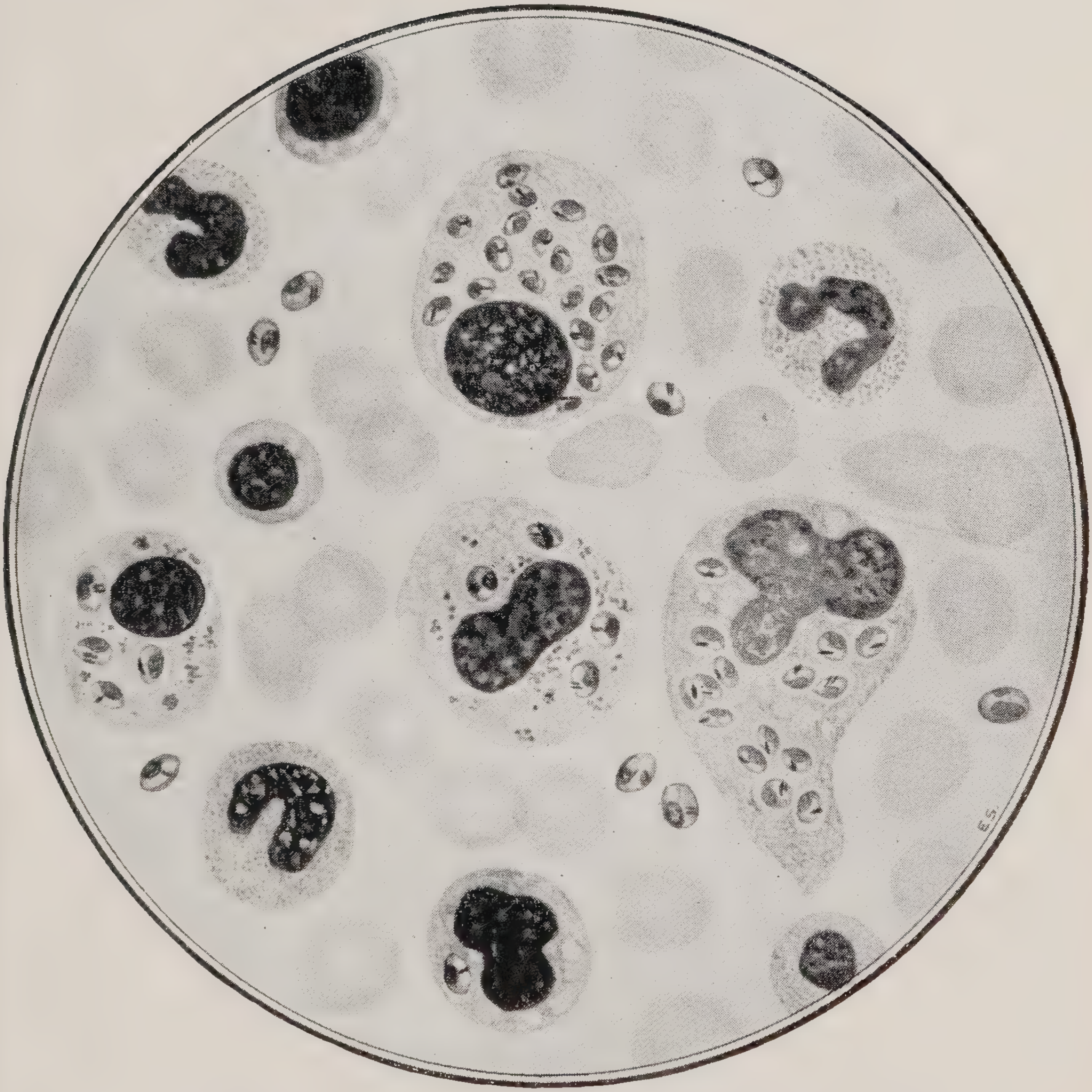
(Manson.)

Plate 19.



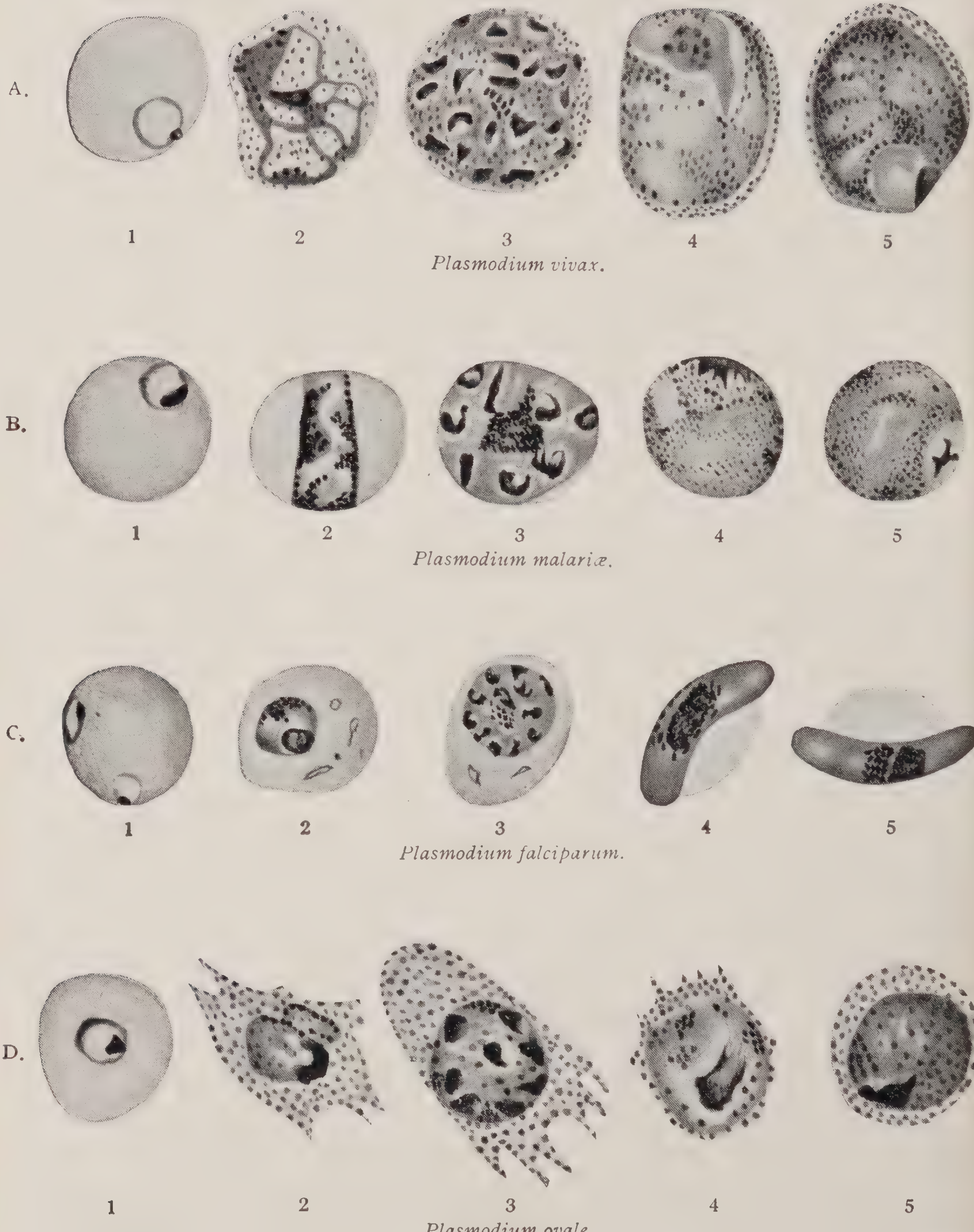
Guinea-worm lying in part superficially and being gently drawn from the subcutaneous tissue of foot. (Partly after Bahr.)

Plate 20.



Scrapings from spleen (Kala-azar). Free and intracellular parasites.
(Wellcome Bureau of Scientific Research.

Plate 21.

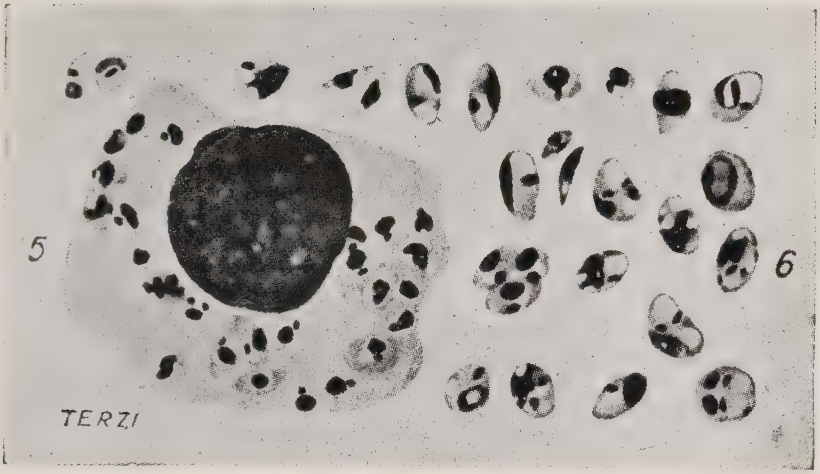


B. Jobling del. (×2000)

Malarial parasites of man.

1. Young ring. 2. Half-grown form. 3. Nearly mature schizont.
4. Male gametocyte. 5. Female gametocyte.

Plate 22.



Leishmania tropica. (After Manson.)

5. Parasites in endothelial cell. 6. Free forms.

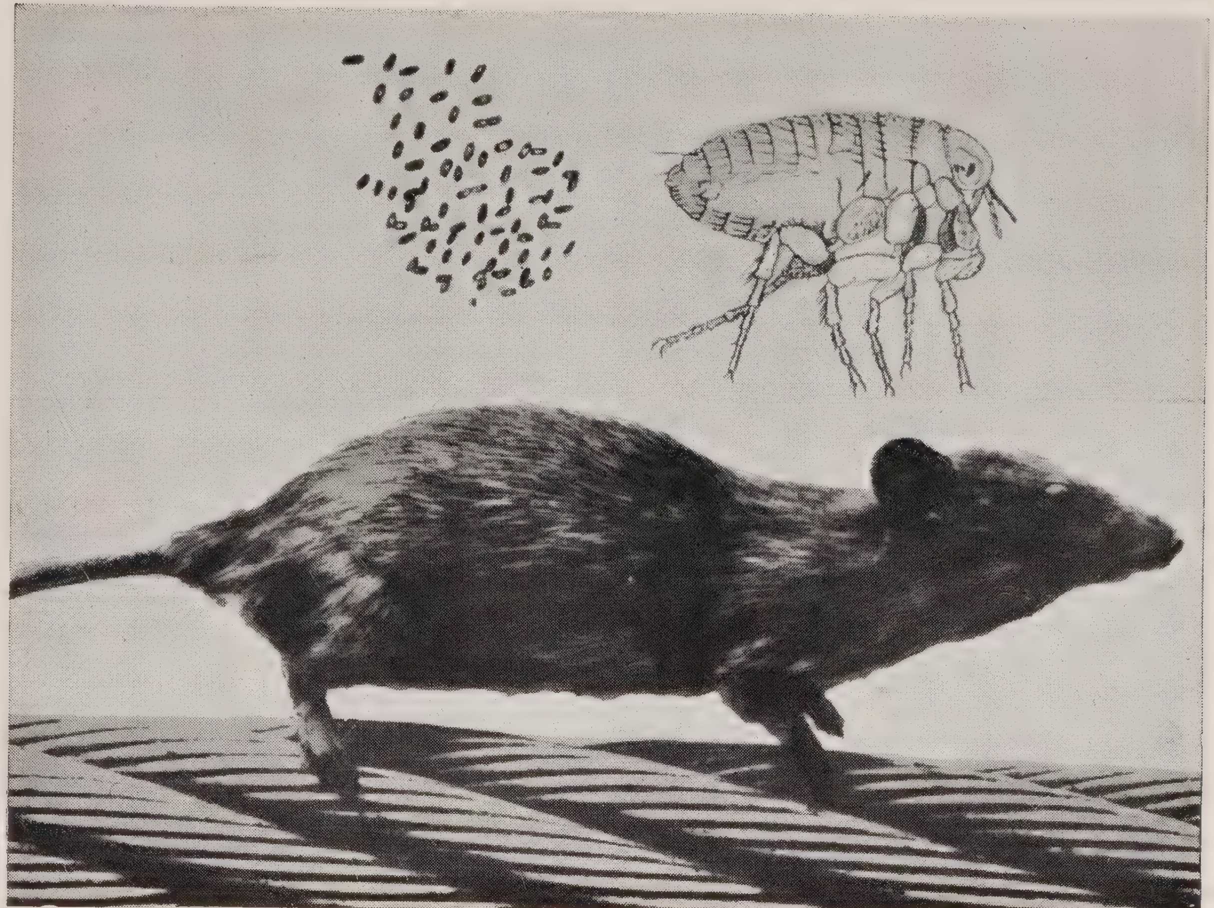
Plate 23.

Oriental sore.

Plate 24.

PELLAGRA.

Showing the symmetrical cutaneous involvement of the distal parts of the limbs, the neck and the face.

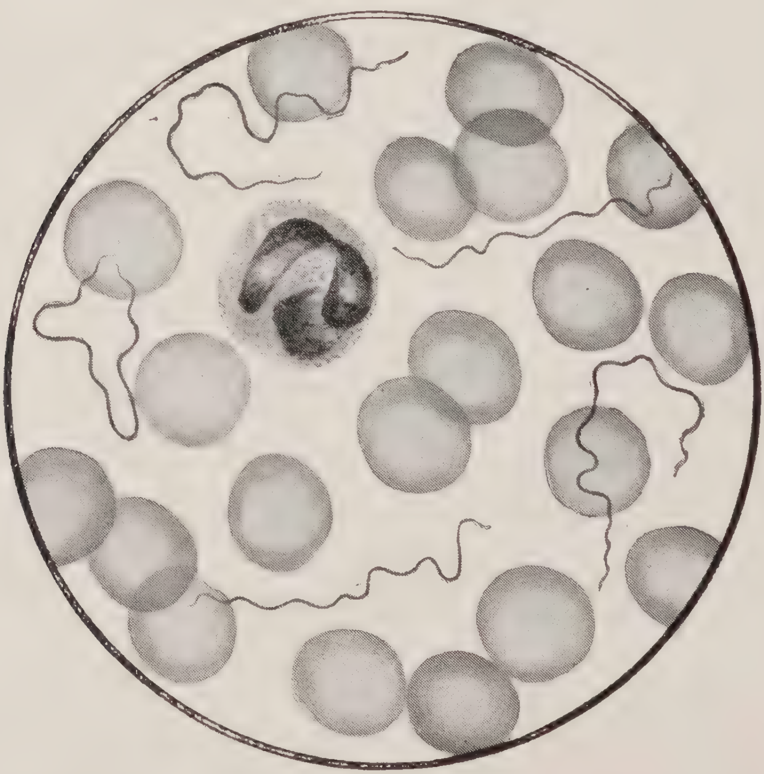


Bacillus pestis ; *Xenopsylla cheopis* (female) and *Rattus rattus*.
(Wellcome Bureau of Scientific Research.)

Plate 26.

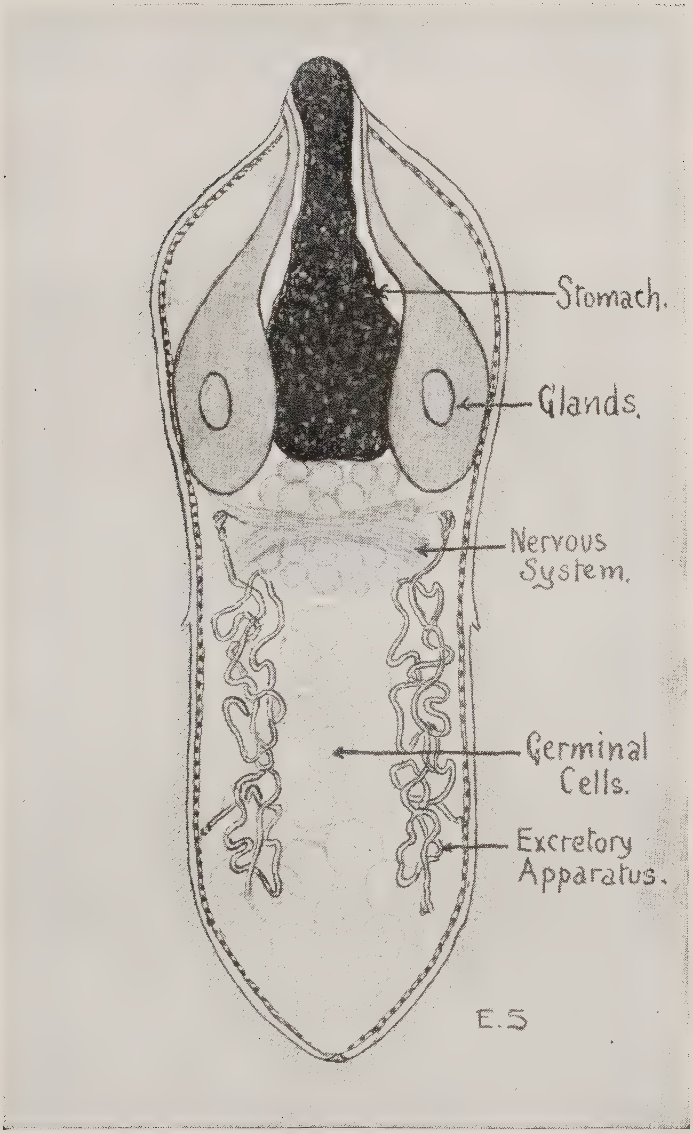
Leptospira icterohæmorrhagiæ. ×3000. Modified after Hideyo Noguchi.
(Wellcome Bureau of Scientific Research.)

Plate 27.



B. Jobling del. *Spirochæta recurrentis.* (×1500)
As seen in Leishman-stained blood film of a case of relapsing fever.

Plate 28.



Miracidium of *Schistosoma hæmatobium.*

(After Sandwith.)

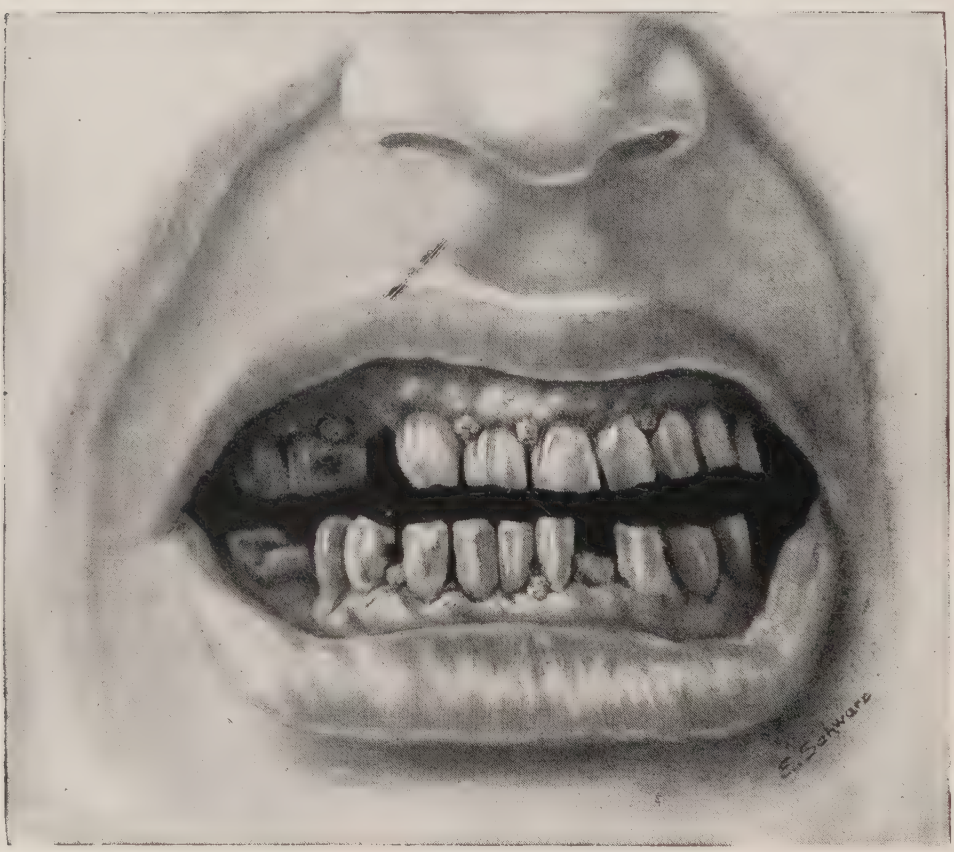
Plate 29.

A. B.

A. *Planorbis boissyi.* B. *Bulinus truncatus.*

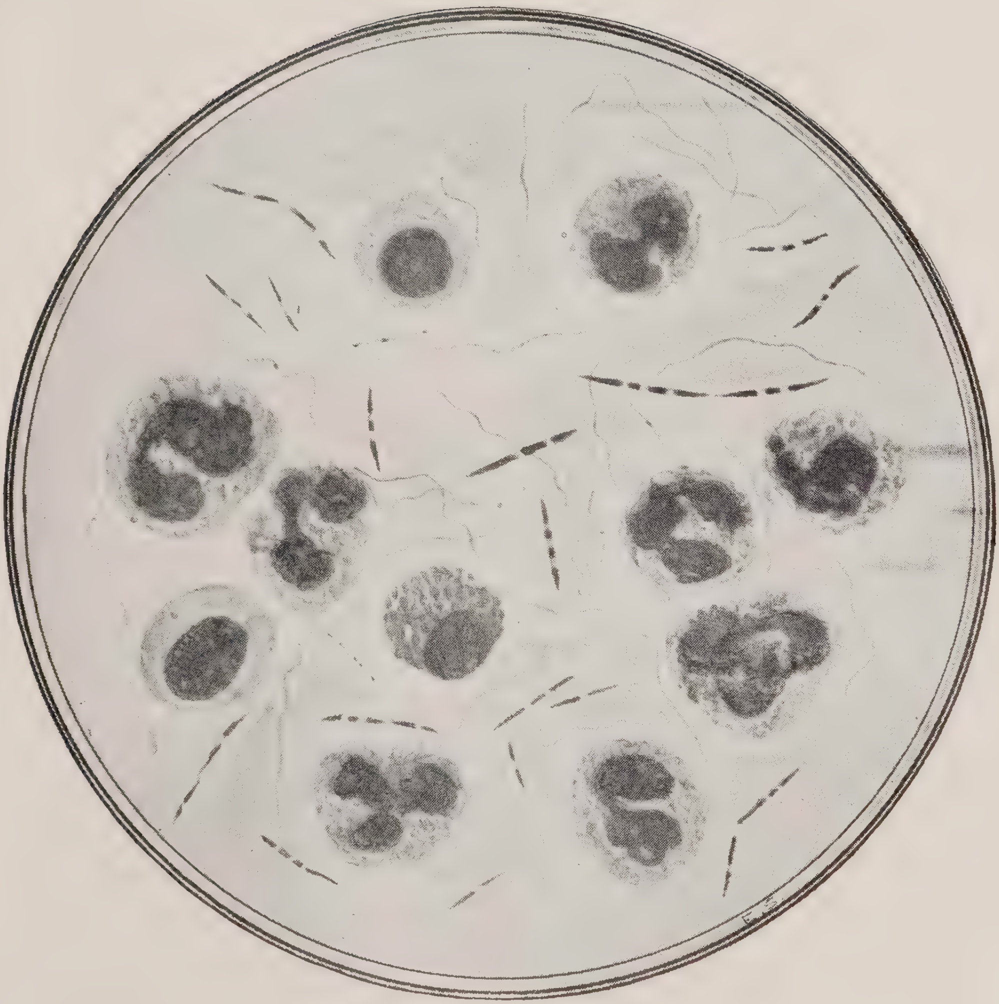
Intermediate hosts of *Schistosoma.*

Plate 30.



Early scurvy showing " buds " approaching the " blossom " stages.
(Wellcome Bureau of Scientific Research.)

Plate 31.



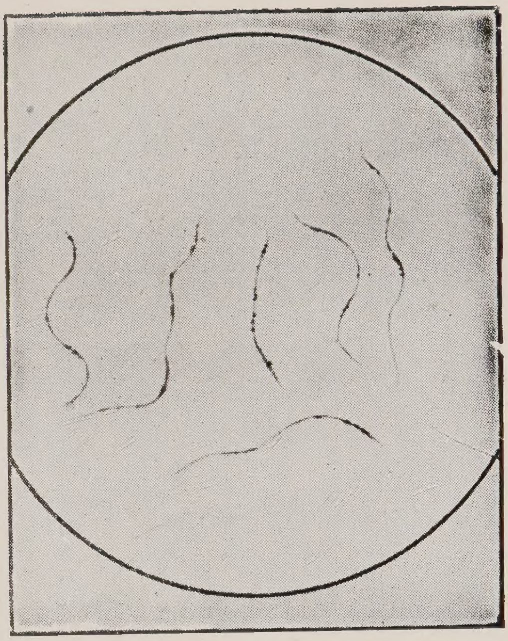
Film from Ulcus tropicum. Smear showing Spirochætes and Fusiform Bacilli.
(Redrawn from Fourth Report, Wellcome Tropical Research Laboratories.)

Plate 32.

(A) Tinea Cruris—Showing typical distribution of the eruption.

(B) Tinea of Axilla—Note the clear-cut, slightly raised, scaling edges of the lesion. These appearances are also typical of untreated Tinea Cruris.

A.—Matted Hair, armpit.

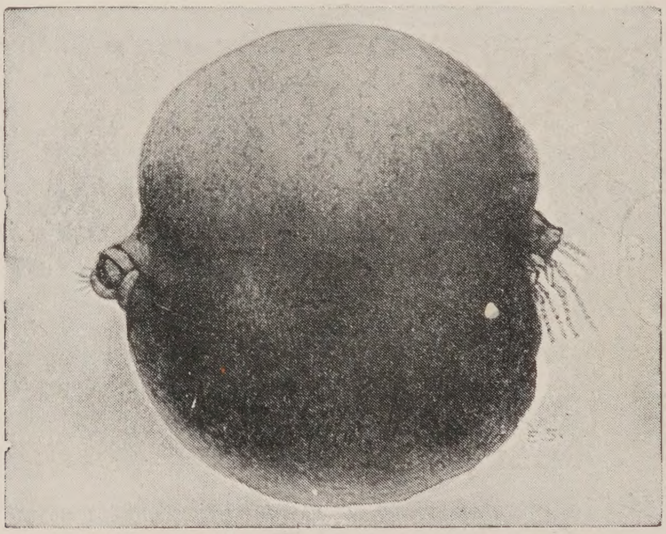


B.—Hair, natural size.

Plate 33.—Trichomycosis.

Plate 34.—1. *T. rubra*. 2. *T. nigra*. 3. *T. flava*.
(Redrawn after Chalmers and O'Farrell.)

A



B

C

Plate 35.—A Chigger Flea, greatly enlarged. B. Female flea with distended abdomen full of ripe eggs. C. Section through chigger *in situ*. (After Karsten.)